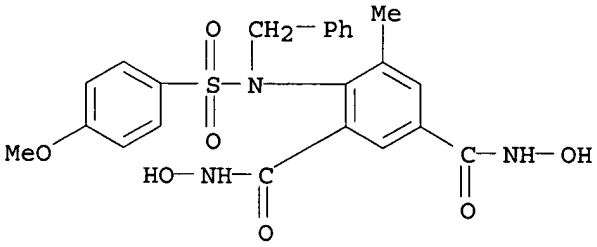
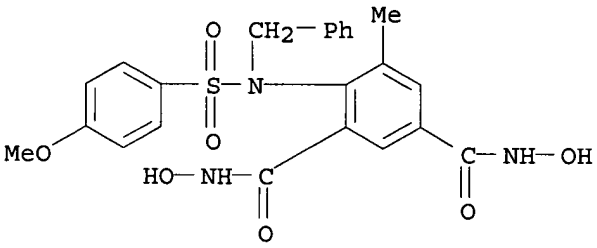
acceptable salts, optical [redacted]mers, and diastereomers. Prepn[redacted] of over 400 compds., including I and their intermediates, are given. For instance, 2-[(4-methoxybenzenesulfonyl)amino]-3-methylbenzoic acid Me ester (prepn. given) was N-alkylated by 3-picolyl chloride-HCl (83%), followed by hydrolysis of the ester with LiOH in aq. THF (100%), activation with oxalyl chloride, and hydroxamidation with NH2OH.HCl (51%), to give title compd. II. At 50 mg/kg/day in rats with cartilage implants, II gave 44.6% inhibition of cartilage wt. loss, and 51.2% inhibition of cartilage collagen loss.

IT **206549-44-2P 206549-45-3P**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(prepn. of ortho-sulfonamido aryl hydroxamic acids as matrix **metalloproteinase** and TACE inhibitors)

RN 206549-44-2 CAPLUS
CN 1,3-Benzenedicarboxamide, N,N'-dihydroxy-4-[[(4-methoxyphenyl)sulfonyl](phenylmethyl)amino]-5-methyl- (9CI) (CA INDEX NAME)



RN 206549-45-3 CAPLUS
CN 1,3-Benzenedicarboxamide, N,N'-dihydroxy-4-[[(4-methoxyphenyl)sulfonyl](phenylmethyl)amino]-5-methyl-, disodium salt (9CI) (CA INDEX NAME)



●2 Na

=> file stnguide

COST IN U.S. DOLLARS	SINCE FILE ENTRY	TOTAL SESSION
FULL ESTIMATED COST	57.82	229.27
DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS)	SINCE FILE ENTRY	TOTAL SESSION
CA SUBSCRIBER PRICE	-7.81	-9.11

FILE 'STNGUIDE' ENTERED AT 10:35:40 ON 16 OCT 2003

Structure attributes must be viewed using STN Express query preparation.

=> s l1
   REGlstRY INITIATED
Substance data SEARCH and crossover from CAS REGISTRY in progress...
Use DISPLAY HITSTR (or FHITSTR) to directly view retrieved structures.

SAMPLE SEARCH INITIATED 10:26:56 FILE 'REGISTRY'
SAMPLE SCREEN SEARCH COMPLETED - 2731 TO ITERATE

 36.6% PROCESSED 1000 ITERATIONS 50 ANSWERS
INCOMPLETE SEARCH (SYSTEM LIMIT EXCEEDED)
SEARCH TIME: 00.00.01

FULL FILE PROJECTIONS: ONLINE **COMPLETE**
BATCH **COMPLETE**
PROJECTED ITERATIONS: 51486 TO 57754
PROJECTED ANSWERS: 8553 TO 11219

L2 50 SEA SSS SAM L1

L3 27 L2

=> s l3 and metalloproteinase enzyme
12942 METALLOPROTEINASE
687014 ENZYME
20 METALLOPROTEINASE ENZYME
(METALLOPROTEINASE(W)ENZYME)
L4 0 L3 AND METALLOPROTEINASE ENZYME

=> s l3 and metalloproteinase enzyme
12942 METALLOPROTEINASE
687014 ENZYME
20 METALLOPROTEINASE ENZYME
(METALLOPROTEINASE(W)ENZYME)
L5 0 L3 AND METALLOPROTEINASE ENZYME

=> s l3 and metalloproteinase
12942 METALLOPROTEINASE
L6 2 L3 AND METALLOPROTEINASE

=> d 1-2 ibib abs hitstr

L6 ANSWER 1 OF 2 CAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 2002:637638 CAPLUS
DOCUMENT NUMBER: 137:185315
TITLE: Isophthalic acid derivatives as matrix **metalloproteinase** inhibitors, and their pharmaceutical compositions and use in the treatment of cancer, arthritis, and congestive heart failure.
INVENTOR(S): Barvian, Nicole Chantel; Connor, David Thomas; Dyer, Richard Dennis; Johnson, Adam Richard; Patt, William Chester
PATENT ASSIGNEE(S): Warner-Lambert Company, USA
SOURCE: PCT Int. Appl., 64 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2002064547	A2	20020822	WO 2002-IB344	20020204
WO 2002064547	A3	20021205		

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM

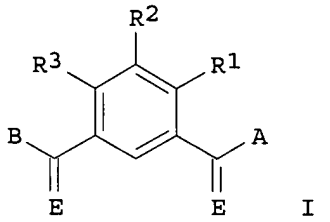
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

US 2002156061	A1	20021024	US 2002-75918	20020213

PRIORITY APPLN. INFO.: US 2001-268736P P 20010214

OTHER SOURCE(S): MARPAT 137:185315

GI



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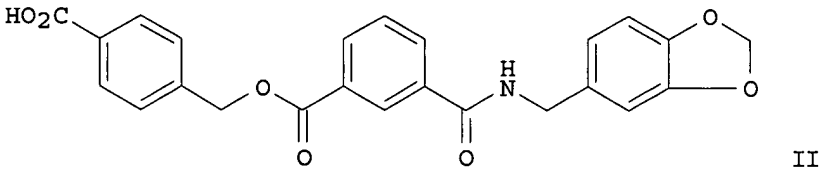


II

AB Selective MMP-13 inhibitors are disclosed, specifically isophthalic acid derivs. I or pharmaceutically acceptable salts thereof [wherein: R1, R2, R3 = H, halo, OH, C1-6 alkyl, C1-6 alkoxy, C2-6 alkenyl, C2-6 alkynyl, NO2, NR4R5, cyano, or CF3; E = O or S; A, B = OR4 or NR4R5; R4, R5 = H, C1-6 alkyl, C2-6 alkenyl, C2-6 alkynyl, (CH2)n-aryl, (CH2)n-cycloalkyl, (CH2)n-heteroaryl; or NR4R5 = (un)substituted 3- to 8-membered ring, optionally contg. an addnl. O, S, or NH; n = 0-6]. The compds. are useful for treating diseases in a mammal that are mediated by MMP enzymes. Specifically claimed uses are treatment of cancer, rheumatoid arthritis, osteoarthritis, and congestive heart failure. Approx. 70 compds. were prepd. and/or claimed. Some of the compds. were prepd.by a combinatorial method. For instance, N-(1,3-benzodioxol-5-ylmethyl)isophthalamic acid was esterified with 4-(bromomethyl)benzoic acid tert-Bu ester using Cs2CO3 in DMF, and the resultant tert-Bu ester function was cleaved with TFA in anisole to give title compd. II. This compd. had IC50 (nM) values as follows: >100,000 for MMP-1; 30,000 for MMP-3; and 33 for MMP-13, thus showing high selectivity for the latter.

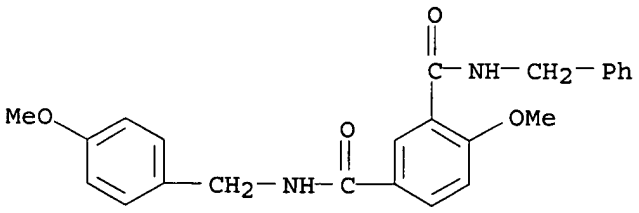
IT **449790-90-3P**, N'-Benzyl-4-methoxy-N-(4-methoxybenzyl)isophthalamide

RL: CPN (Combinatorial preparation); PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); CMBI (Combinatorial study); PREP (Preparation); USES (Uses)

(drug candidate; prepn. and use of isophthalic acid derivs. as selective MMP-13 inhibitors)

RN 449790-90-3 CAPLUS

CN 1,3-Benzenedicarboxamide, [redacted]ethoxy-N1-[(4-methoxyphenyl)me 1]-N3-(phenylmethyl)- (9CI) (CA INDEX NAME)



L6 ANSWER 2 OF 2 CAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 2002:637472 CAPLUS
DOCUMENT NUMBER: 137:201321
TITLE: Preparation of substituted isophthalic acid derivatives, multicyclic pyrimidinediones and analogs thereof as matrix **metalloproteinase** inhibitors
INVENTOR(S): Andrianjara, Charles; Ortwine, Daniel Fred; Pavlovsky, Alexander Gregory; Roark, William Howard
PATENT ASSIGNEE(S): Warner-Lambert Company, USA
SOURCE: PCT Int. Appl., 173 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

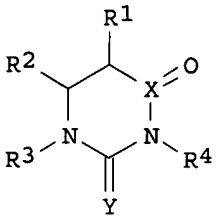
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2002064080	A2	20020822	WO 2002-IB447	20020213
WO 2002064080	A3	20021212		

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM

RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

US 2003078276	A1	20030424	US 2002-75069	20020213

PRIORITY APPLN. INFO.: US 2001-268821P P 20010214
GI



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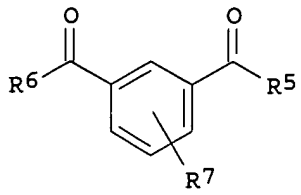
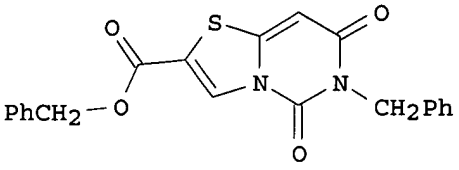


II



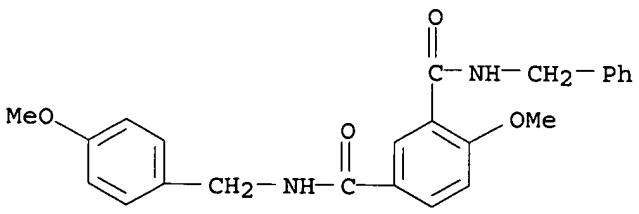
III

AB Title compds., I [R1 and R2 together may form a substituted arom. ring or a heterocyclic ring; or R2 and R3 together may form substituted heterocycle; or R1, R3, or R4 = alkyl, arylalkyl, etc.; X = C, S; Y = O, N with provision when Y = N it forms a 5-membered heterocycle with R3] and II [R5, R6 = arylalkylamine, heterocyclylalkoxy, etc.; R7 = H, MeO, NO2, etc.], are prepd. and disclosed as matrix **metalloproteinase** (MMP) inhibitors. Thus, III was prepd. in five steps via cyclocondensation of diethylmalonate and benzylurea with subsequent chlorination, substitution with hydrosulfide hydrate to form an in situ intermediate that was reacted with bromoacetaldehyde dimethylacetal, followed by acid catalyzed cyclization and substitution with benzylchloroformate. III was demonstrated to inhibit MMP13 with an IC50 value (in .mu.M) of 0.0230. I and II bind allosterically to the catalytic domain of MMP-13 and comprise a hydrophobic group, first and second hydrogen bond acceptors and at least one, and preferably both, of a third hydrogen bond acceptor and a second hydrophobic group. Cartesian coordinates for centroids of the above features are defined in the specification. When the ligand binds to MMP-13, the first, second and third (when present) hydrogen bond acceptors bond resp. with Thr245, Thr247 and Met 253, the first hydrophobic group locates within the S1' channel of MMP-13 and the second hydrophobic group (when present) is relatively open to solvent. The compds. specifically inhibit the matrix **metalloproteinase**-13 enzyme and thus are useful for treating diseases resulting from tissue breakdown, such as heart disease, multiple sclerosis, arthritis, atherosclerosis, and osteoporosis.

IT **449790-90-3P**
RL: CPN (Combinatorial preparation); PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); CMBI (Combinatorial study); PREP (Preparation); USES (Uses)
(combinatorial prepn. and pharmaceutical activity of substituted isophthalic acid derivs. as matrix **metalloproteinase** inhibitors)

RN 449790-90-3 CAPLUS

CN 1,3-Benzenedicarboxamide, 4-methoxy-N1-[(4-methoxyphenyl)methyl]-N3-(phenylmethyl)- (9CI) (CA INDEX NAME)



L9 ANSWER 8 OF 12 CAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 2001:47677 CAPLUS
DOCUMENT NUMBER: 134:246978
TITLE: Disruption of matrix **metalloproteinase** 2 binding to integrin .alpha.v.beta.3 by an organic molecule inhibits angiogenesis and tumor growth in vivo
AUTHOR(S): Silletti, Steve; Kessler, Torsten; Goldberg, Joel; Boger, Dale L.; Cheresh, David A.
CORPORATE SOURCE: Departments of Immunology and Vascular Biology, The Scripps Research Institute, La Jolla, CA, 92037, USA
SOURCE: Proceedings of the National Academy of Sciences of the United States of America (2001), 98(1), 119-124
CODEN: PNASA6; ISSN: 0027-8424
PUBLISHER: National Academy of Sciences
DOCUMENT TYPE: Journal
LANGUAGE: English

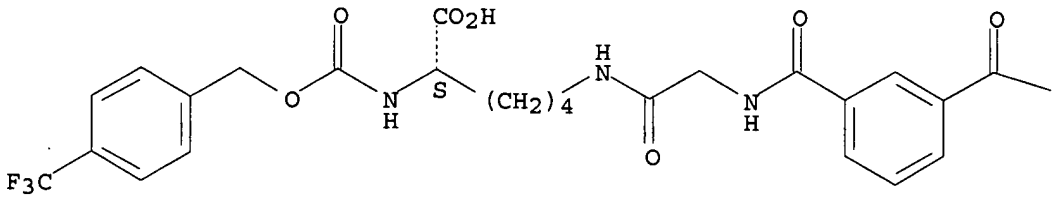
AB Matrix **metalloproteinase** 2 (MMP2) can assoc. with integrin .alpha.v.beta.3 on the surface of endothelial cells, thereby promoting vascular invasion. Here, we describe an org. mol. (TSRI265) selected for its ability to bind to integrin .alpha.v.beta.3 and block .alpha.v.beta.3 interaction with MMP2. Although disrupting .alpha.v.beta.3/MMP2 complex formation, TSRI265 has no effect on .alpha.v.beta.3 binding to its extracellular matrix ligand vitronectin and does not influence MMP2 activation or catalytic activity directly. However, TSRI265 acts as a potent antiangiogenic agent and thereby blocks tumor growth in vivo. These findings suggest that activated MMP2 does not facilitate vascular invasion during angiogenesis unless it forms a complex with .alpha.v.beta.3 on the endothelial cell surface. By disrupting endothelial cell invasion without broadly suppressing cell adhesion or MMP function, the use of compds. such as TSRI265 may provide a novel therapeutic approach for diseases assocd. with uncontrolled angiogenesis.

IT **331678-22-9**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(disruption of matrix **metalloproteinase** 2 binding to integrin .alpha.v.beta.3 by org. mol. (TSRI265), inhibits angiogenesis and tumor growth in vivo)

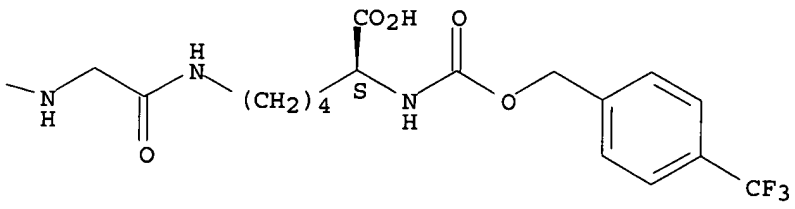
RN 331678-22-9 CAPLUS
CN L-Lysine, N6,N6'-[1,3-phenylenebis[carbonylimino(1-oxo-2,1-ethanediyl)]]bis[N2-[[[4-(trifluoromethyl)phenyl]methoxy]carbonyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



PAGE 1-B



REFERENCE COUNT: 22 THERE ARE 22 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L9 ANSWER 9 OF 12 CAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 2000:456916 CAPLUS
DOCUMENT NUMBER: 133:68929
TITLE: Use of a matrix **metalloproteinase** inhibitor and an integrin antagonist in the treatment of neoplasia
INVENTOR(S): McKearn, John P.; Gordon, Gary; Cunningham, James J.; Gately, Stephen T.; Koki, Alane T.; Masferrer, Jaime L.
PATENT ASSIGNEE(S): G. D. Searle & Co., USA
SOURCE: PCT Int. Appl., 358 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 12
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2000038719	A1	20000706	WO 1999-US30700	19991222
W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
CA 2356402	AA	20000706	CA 1999-2356402	19991222
EP 1140183	A1	20011010	EP 1999-968942	19991222
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
JP 2002533407	T2	20021008	JP 2000-590670	19991222
ZA 2001005055	A	20020920	ZA 2001-5055	20010620
ZA 2001005120	A	20020107	ZA 2001-5120	20010621

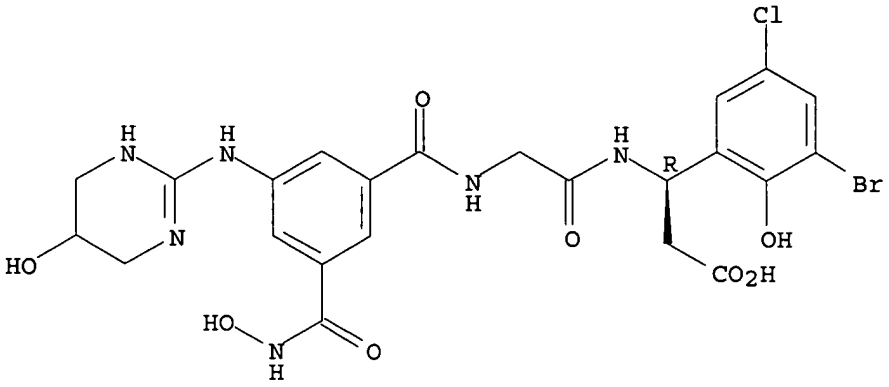
PRIORITY APPLN. INFO.: US 1998-113786P P 19981223
WO 1999-US30700 W 19991222

AB Methods are provided to treat or prevent neoplasia disorders in a mammal using a combination of a matrix **metalloproteinase** inhibitor, an integrin antagonist, and an antineoplastic agent.

IT **280105-14-8**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(matrix **metalloproteinase** inhibitor and integrin antagonist in neoplasia treatment)

RN 280105-14-8 CAPLUS
CN .beta.-Alanine, N-[3-[(hydroxyamino)carbonyl]-5-[(1,4,5,6-tetrahydro-5-hydroxy-2-pyrimidinyl)amino]benzoyl]glycyl-3-(3-bromo-5-chloro-2-hydroxyphenyl)-, (3R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

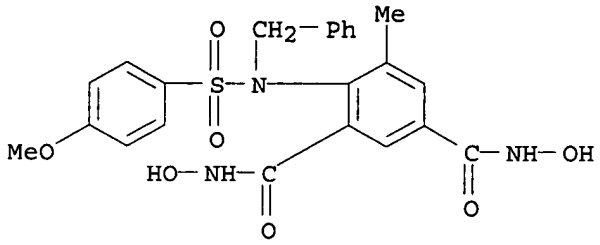


REFERENCE COUNT: 5 THERE ARE 5 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L9 ANSWER 10 OF 12 CAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 1999:495123 CAPLUS
DOCUMENT NUMBER: 131:129760
TITLE: Preparation of sulfonamidobenzenehydroxamates and analogs as matrix **metalloproteinase** and TACE inhibitors
INVENTOR(S): Levin, Jeremy Ian; Du, Mila T.; Venkatesan, Aranapakam Mudumbai; Nelson, Frances Christy; Zask, Arie; Gu, Yansong
PATENT ASSIGNEE(S): American Cyanamid Co., USA
SOURCE: U.S., 68 pp.
CODEN: USXXAM
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

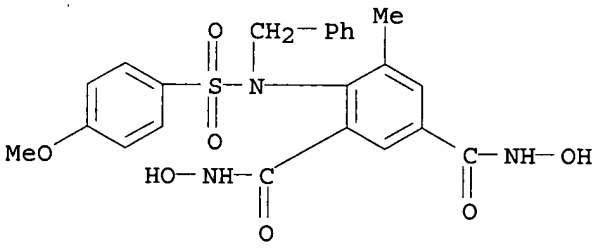
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 5929097	A	19990727	US 1997-944593	19971006

PRIORITY APPLN. INFO.: US 1996-28504P P 19961016
OTHER SOURCE(S): MARPAT 131:129760
AB RSO2N(CH2R7)ZCONHOH [I; R = (un)substituted (hetero)aryl; R7 = H, alkyl, Ph, etc.; Z = (un)substituted phenylene or -naphthylene] were prepd. Thus, 2-(H2N)C6H4CO2Me was amidated by 4-(MeO)C6H4SO2Cl and the N-benzylated product converted in 2 steps to I [R = C6H4(OMe)-4, R7 = Ph, Z = 1,2-phenylene]. Data for biol. activity of I were given.
IT **206549-45-3P**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(prepn. of sulfonamidobenzenehydroxamates and analogs as matrix **metalloproteinase** and TACE inhibitors)
RN 206549-45-3 CAPLUS
CN 1,3-Benzenedicarboxamide, N,N'-dihydroxy-4-[[(4-methoxyphenyl)sulfonyl](phenylmethyl)amino]-5-methyl-, disodium salt (9CI) (CA INDEX NAME)



●2 Na

IT **206549-44-2P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(prepn. of sulfonamidobenzenehydroxamates and analogs as matrix **metalloproteinase** and TACE inhibitors)
RN 206549-44-2 CAPLUS
CN 1,3-Benzenedicarboxamide, N,N'-dihydroxy-4-[[(4-methoxyphenyl)sulfonyl](phenylmethyl)amino]-5-methyl- (9CI) (CA INDEX NAME)



REFERENCE COUNT: 19 THERE ARE 19 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L9 ANSWER 11 OF 12 CAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 1999:96248 CAPLUS
DOCUMENT NUMBER: 130:148689
TITLE: Phosphonated agents and their antiangiogenic and antitumorigenic use
INVENTOR(S): Collins, Delwood C.; Gagliardi, Antonio R.; Nickel, Peter
PATENT ASSIGNEE(S): University of Kentucky Research Foundation, USA
SOURCE: PCT Int. Appl., 74 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9905148	A1	19990204	WO 1998-US15470	19980724
W: AU, CA, JP, MX				
RW: AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
AU 9885915	A1	19990216	AU 1998-85915	19980724
AU 739637	B2	20011018		
EP 1019419	A1	20000719	EP 1998-937133	19980724
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI				

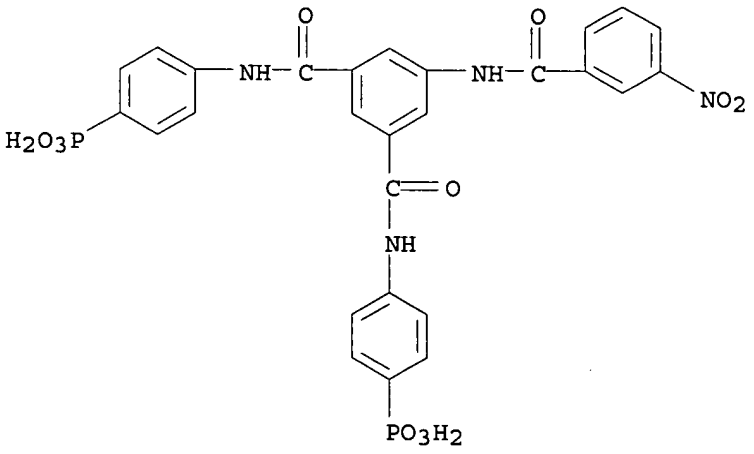
PRIORITY APPLN. INFO.: US 1997-899996 A 19970724
WO 1998-US15470 W 19980724
OTHER SOURCE(S): MARPAT 130:148689

AB The present invention relates to novel phosphonic acid substituted agents and their pharmaceutical compns. Phosphonic acid substituted agents that are potent inhibitors of angiogenesis or tumorigenesis is defined by the following formula: (P-Yn1)m1-Q1-K-(Q2-(Yn2-P)m2)j (P = phosphonic group, phosphonic salt; Y = OCO, NR1CO, CON(R1)R2; Q1, Q2 = aryl; K = H, NHCONH, NHCSNH, NHCOR3, NHCSR3CSNH; j, n1, n2 = 0-2; m1, m2 = 1-4; R1 = H, CH2CO2H, alkyl; R2 = alkyl, aryl, alkaryl; R3 = aryl). A pharmaceutical compn. for the treatment of angiogenesis-dependent conditions or tumors comprises an effective amt. of a phosphonic acid agent and a pharmaceutically acceptable carrier. Some of the phosphonic acid agents were more potent inhibitors of angiogenesis in the chick chorioallantoic membrane (CAM) assay and to human microvascular endothelial cell growth than suramin.

IT **220240-01-7**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(phosphonic acid agents and their antiangiogenic and antitumorigenic use)

RN 220240-01-7 CAPLUS

CN Phosphonic acid, [[5-[(3-nitrobenzoyl)amino]-1,3-phenylene]bis(carbonylimino-4,1-phenylene)]bis-, disodium salt (9CI) (CA INDEX NAME)



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REFERENCE COUNT: 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L9 ANSWER 12 OF 12 CAPLUS COPYRIGHT 2003 ACS on STN

ACCESSION NUMBER: 1998:251153 CAPLUS
DOCUMENT NUMBER: 128:308308
TITLE: The preparation and use of ortho-sulfonamido aryl hydroxamic acids as matrix **metalloproteinase** and TACE inhibitors
INVENTOR(S): Levin, Jeremy Ian; Du Mila, T.; Venkatesan, Aranapakam Mudumbai; Nelson, Frances Christy; Zask, Arie; Gu, Yansong
PATENT ASSIGNEE(S): American Cyanamid Company, USA
SOURCE: PCT Int. Appl., 164 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
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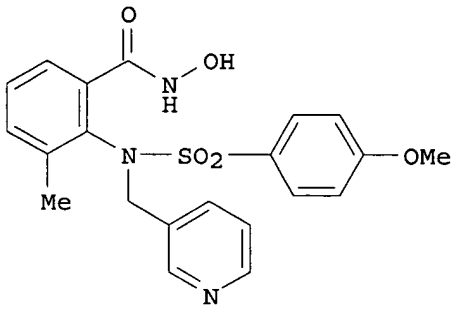
WO 9816503	A2	19980423	WO 1997-US18280	19971008
W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, HU, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, UZ, VN, YU, ZW				
RW: GH, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
AU 9851458	A1	19980511	AU 1998-51458	19971008
AU 731737	B2	20010405		
EP 938471	A1	19990901	EP 1997-946246	19971008
EP 938471	B1	20011212		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, PT, IE, SI, LT, LV, FI, RO				
BR 9712525	A	19991019	BR 1997-12525	19971008
CN 1240429	A	20000105	CN 1997-180613	19971008
JP 2001504809	T2	20010410	JP 1998-518448	19971008
AT 210637	E	20011215	AT 1997-946246	19971008
ES 2166102	T3	20020401	ES 1997-946246	19971008
ZA 9709233	A	19990415	ZA 1997-9233	19971015
TW 410220	B	20001101	TW 1997-86114187	19971015
KR 2000049196	A	20000725	KR 1999-703294	19990415
HK 1021178	A1	20020404	HK 2000-100090	20000106

PRIORITY APPLN. INFO.: US 1996-732631 A 19961016
WO 1997-US18280 W 19971008

OTHER SOURCE(S): MARPAT 128:308308

GI



II

AB The invention relates to novel, low mol. wt., non-peptide inhibitors of matrix metalloproteinases (e.g. gelatinases, stromelysins and collagenases) and TNF-.alpha. converting enzyme (TACE, tumor necrosis factor-.alpha. converting enzyme). The compds. are useful for the treatment of diseases in which these enzymes are implicated such as arthritis, tumor growth and metastasis, angiogenesis, tissue ulceration, abnormal wound healing, periodontal disease, bone disease, proteinuria, aneurysmal aortic disease, degenerative cartilage loss following traumatic joint injury, demyelinating diseases of the nervous system, graft rejection, cachexia, anorexia, inflammation, fever, insulin resistance, septic shock, congestive heart failure, inflammatory disease of the central nervous system, inflammatory bowel disease, HIV infection, age related macular degeneration, diabetic retinopathy, proliferative vitreoretinopathy, retinopathy of prematurity, ocular inflammation, keratoconus, Sjogren's syndrome, myopia, ocular tumors, and ocular angiogenesis/neovascularization. The invention compds. are represented by the formula ZSO2N(CH2R7)ACONHOH [I; A = (un)substituted Ph or naphthyl; Z = (un)substituted aryl, heteroaryl, or benzo-fused heteroaryl; R7 = H, (un)substituted alk(en/yn)yl, Ph, naphthyl, 5- or 6-membered heteroaryl, cycloalkyl, or cycloheteroalkyl; or R7CH2NA forms a non-arom. 1,2-benzo-fused 7- to 10-membered heterocyclic ring with an optional addn. benzo fusion; where the hydroxamic acid moiety and the sulfonamido moiety are bonded to adjacent carbons on group A], and include pharmaceutically

FILE CONTAINS CURRENT INFORMATIO
LAST RELOADED: Oct 10, 2003 (20031010/UP).

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L7 10084 SEA SSS FUL L1

L8 6972 L7

=> s l8 and metalloproteinase
12942 METALLOPROTEINASE
L9 12 L8 AND METALLOPROTEINASE

=> d 1-12 ibib abs hitstr

L9 ANSWER 1 OF 12 CAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 2003:201542 CAPLUS
DOCUMENT NUMBER: 138:217443
TITLE: Rapid identification and classification of metalloenzyme inhibitors using ligands to the functional metal cation
INVENTOR(S): Dyer, Richard Dennis; Hupe, Donald John; Johnson, Adam Richard
PATENT ASSIGNEE(S): Warner-Lambert Company, USA
SOURCE: Eur. Pat. Appl., 17 pp.
CODEN: EPXXDW
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

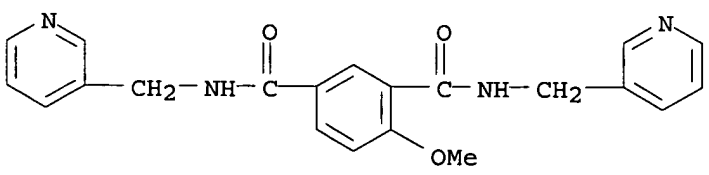
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
EP 1291439	A2	20030312	EP 2002-255715	20020815
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, SK				
US 2003129672	A1	20030710	US 2002-206479	20020726
JP 2003079394	A2	20030318	JP 2002-251608	20020829

PRIORITY APPLN. INFO.: US 2001-315594P A 20010829

AB The present invention is a method for identifying a compd. as a competitive, noncompetitive, or uncompetitive inhibitor of an enzyme having a functional metal cation. The method comprises assaying the compd. for inhibition of the enzyme in the presence of a ligand to the functional metal cation. The ratio (IC50 of the inhibitor with the metalloenzyme in the presence of ligand) divided by (IC50 of the compd. with the metalloenzyme in the presence of ligand) is less than 1 for noncompetitive or uncompetitive inhibitors; if the ratio is equal to 1, the inhibitor is noncompetitive, and if the ratio is >1, the inhibitor is competitive. Thus, synergistic inhibition of matrix metalloproteinases MMP-2, MMP-9, and MMP-13 by noncompetitive inhibitor N-[(3-phenylisoxazol-4-ylmethyl)aminothiocarbonyl]benzamide gave IC50 ratios of 0.1, 0.39, and 0.09, resp., in the presence or absence of acetohydroxamic acid as ligand. The method provides rapid and easy identification of competitive, noncompetitive, or uncompetitive inhibitors of a metalloenzyme, and avoids laborious and time-consuming enzyme kinetics expts.

IT **32828-81-2**
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(metalloproteinases inhibition by; rapid identification and classification of metalloenzyme inhibitors using ligands to the functional metal cation)

RN 32828-81-2 CAPLUS
CN 1,3-Benzenedicarboxamide, 4-methoxy-N,N'-bis(3-pyridinylmethyl)- (9CI) (CA INDEX NAME)



L9 ANSWER 2 OF 12 CAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 2003:5730 CAPLUS
DOCUMENT NUMBER: 138:66669
TITLE: Exponential pattern recognition-based cellular targeting, compositions, methods and anticancer applications
INVENTOR(S): Glazier, Arnold
PATENT ASSIGNEE(S): Drug Innovation & Design, Incorporated, USA
SOURCE: PCT Int. Appl., 157 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2003000201	A2	20030103	WO 2002-US20279	20020624
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
US 2003031677	A1	20030213	US 2002-179610	20020624

PRIORITY APPLN. INFO.: US 2001-300805P P 20010625

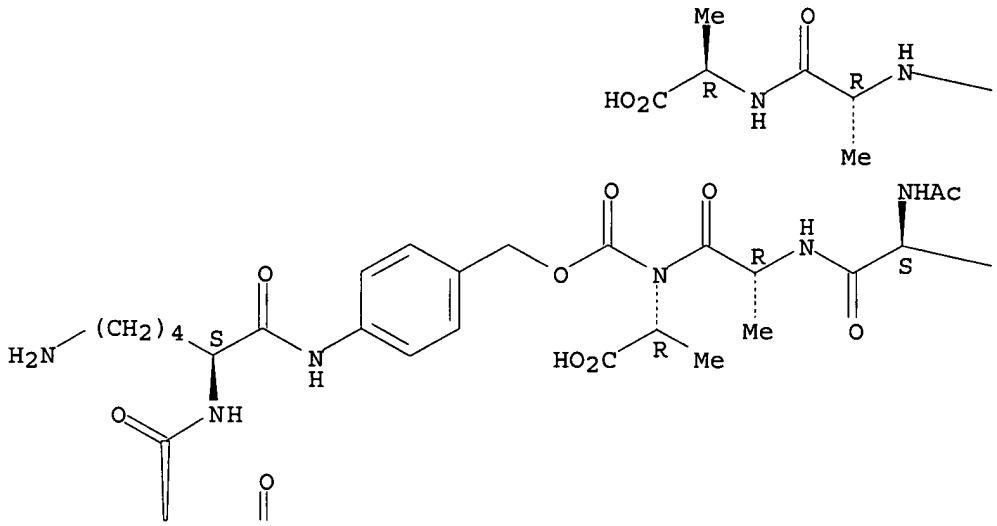
AB The present invention relates to the compns., methods, and applications of a new approach to pattern recognition-based targeting by which an exponential amplification of effector response can be specifically obtained at a targeted cells. The purpose of this invention is to enable the selective delivery of large quantities of an array of effector mols. to target cells for diagnostic or therapeutic purposes. The invention is comprised of two components designated as "Compd. 1" and "Compd. 2": Compd. 1 is comprised of a cell binding agent and a masked female adaptor. Compd. 2 is comprised of a male ligand, an effector agent, and two or more masked female receptors. The male ligand is selected to bind with high affinity to the female adaptor. Compd. 1 can bind with high affinity to the target cell and the female receptor can then be unmasked by an enzyme enriched at the tumor cell. The male ligand of Compd. 2 can then bind to the unmasked female adaptor bound to the target cell. The masked female adaptor on the bound Compd. 2 can then be specifically unmasked. One receptor has in effect become two. Two new mols. of Compd. 2 can bind to the unmasked adaptors receptors. After unmasking two receptors in effect become four. The process can continue in an explosive exponential-like fashion resulting in enormous amplification of the no. of effector mols. specifically deposited at the target cell.

IT **480425-46-5 480425-46-5D**, indanocine-vancomycin derivs.
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(exponential pattern recognition-based cellular targeting compns. for cancer diagnosis or therapy)

RN 480425-46-5 CAPLUS

CN D-Alanine, N2-acetyl-N6-[3,5-dicarboxy-4-[[(55S,59S)-55,59,61-tricarboxy-30-[25-methyl-3,23-dioxo-27-(1-piperidinyl)-2,7,10,13,16,19-hexaoxa-4,22,25-triazaheptacos-1-yl]-7,27,32,52,57-pentaoxo-3,11,14,17,20,23,28,31,36,39,42,45,48-tridecaoxa-6,8,26,33,51,56,58-heptaazahenhexacont-1-yl]amino]benzoyl]-L-lysyl-D-alanyl-N-[[[4-[(D-valyl-L-leucyl-L-lysyl)amino]phenyl]methoxy]carbonyl]-, (13.fwdarw.1'')(15.fwdarw.1''')-diamide with N2-acetyl-L-lysyl-D-alanyl-D-alanine (9CI) (CA INDEX NAME)

Absolute stereochemistry.



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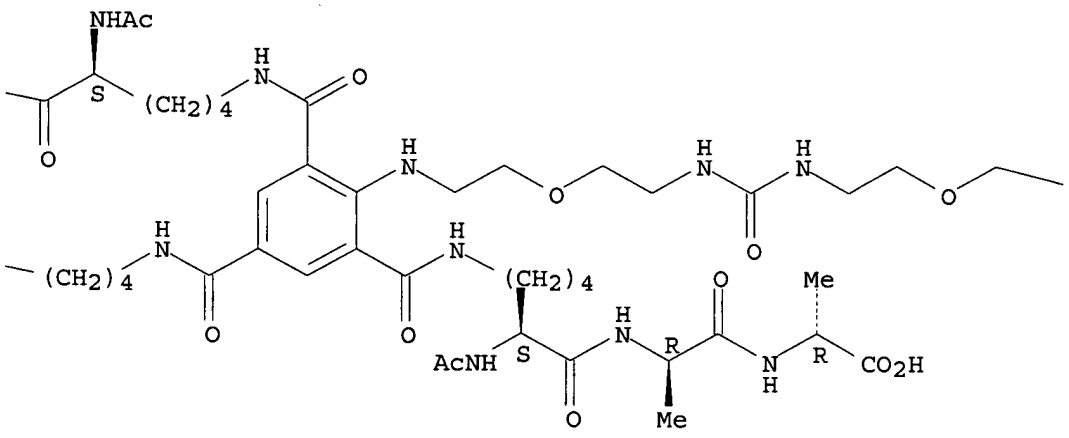

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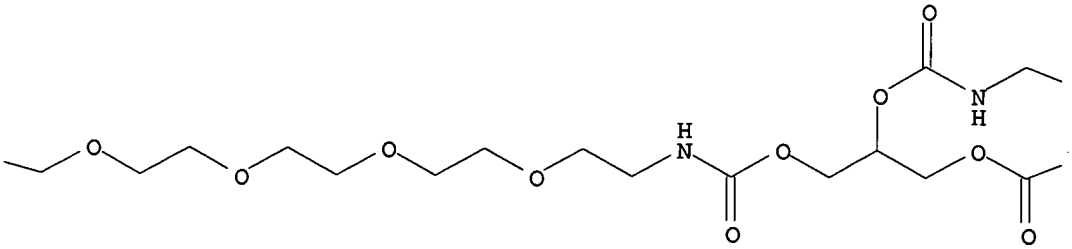

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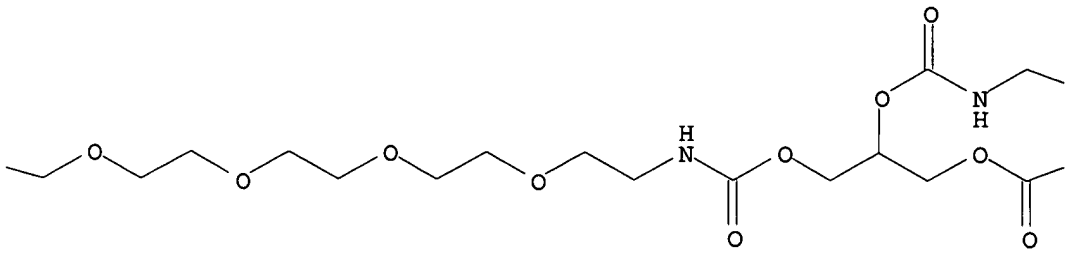

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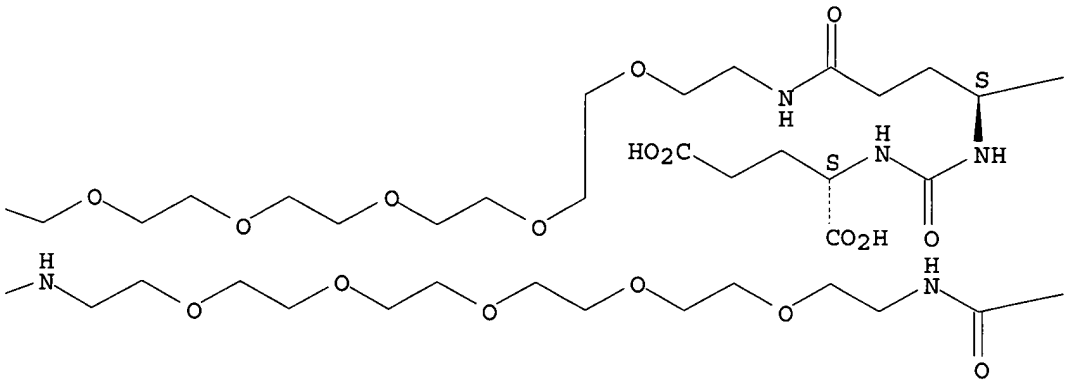

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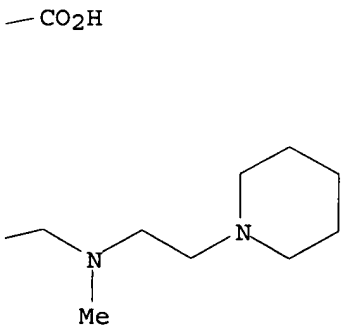

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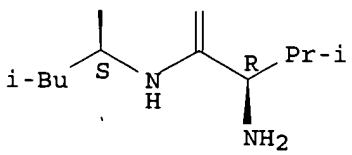
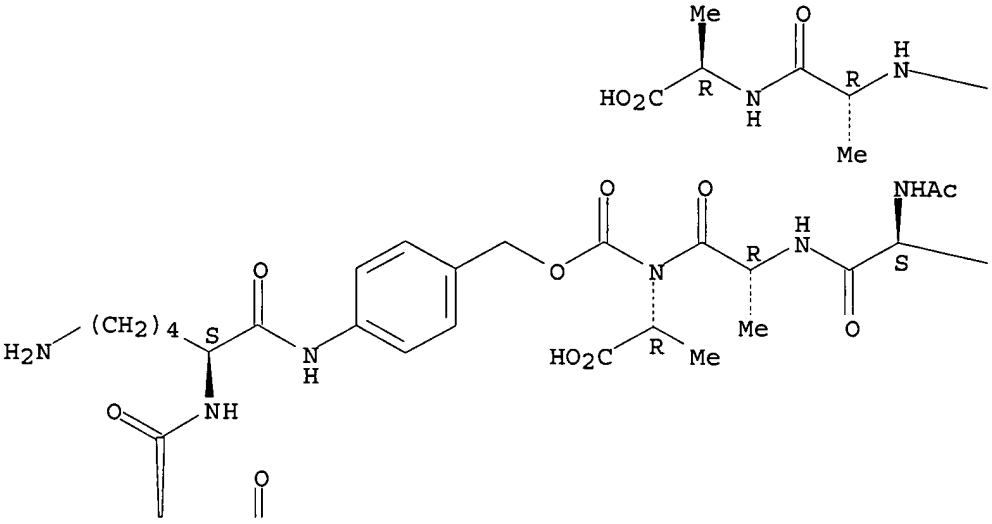


RN 480425-46-5 CAPLUS
CN D-Alanine, N2-acetyl-N6-[3,5-dicarboxy-4-[[(55S,59S)-55,59,61-tricarboxy-30-[25-methyl-3,23-dioxo-27-(1-piperidinyl)-2,7,10,13,16,19-hexaoxa-4,22,25-triazaheptacos-1-yl]-7,27,32,52,57-pentaoxo-

3,11,14,17,20,23,28,31,36,[redacted]42,45,48-tridecaoxa-6,8,26,33,[redacted]56,58-heptaazahenhexacont-1-yl]amino]benzoyl]-L-lysyl-D-alanyl-N-[[[4-[(D-valyl-L-leucyl-L-lysyl)amino]phenyl]methoxy]carbonyl]-, (13.fwdarw.1'')(15.fwdarw.1''')-diamide with N2-acetyl-L-lysyl-D-alanyl-D-alanine (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



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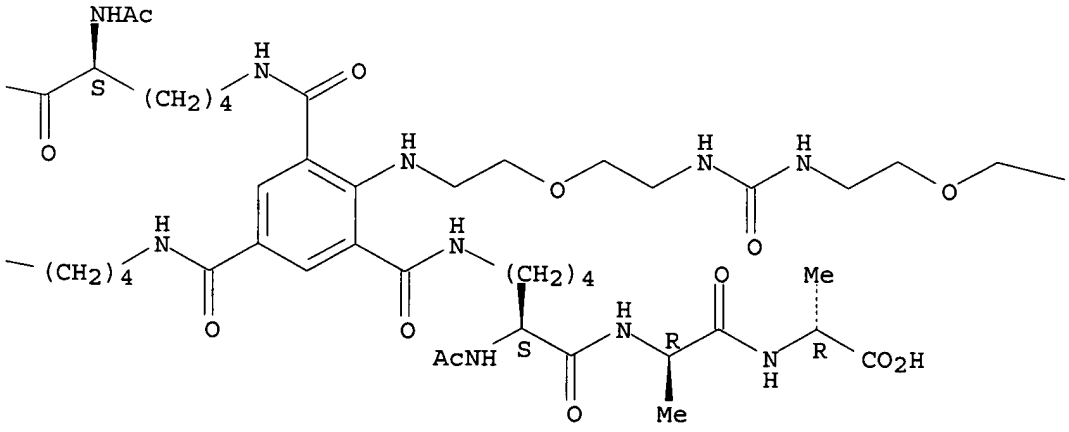

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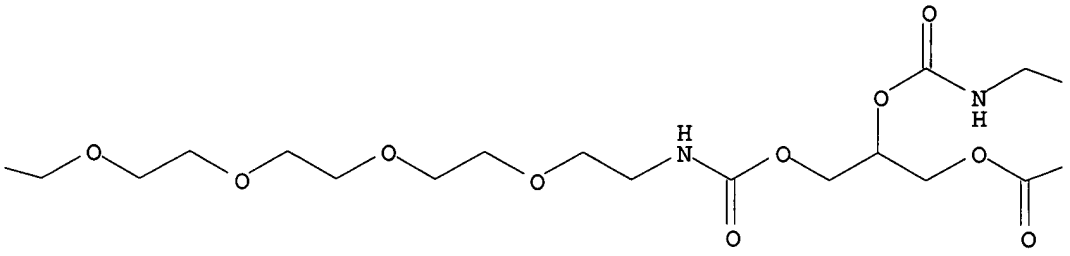

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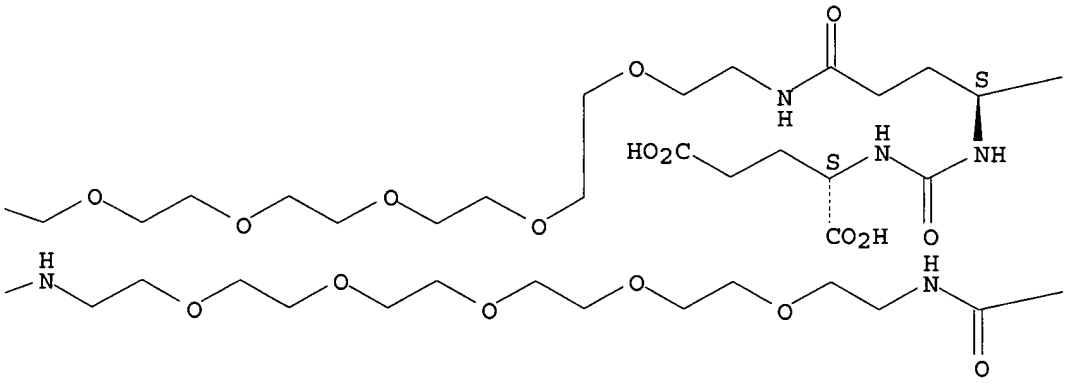

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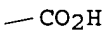

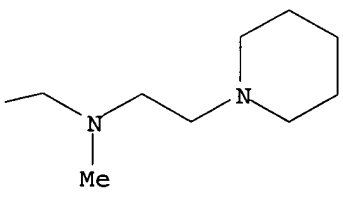

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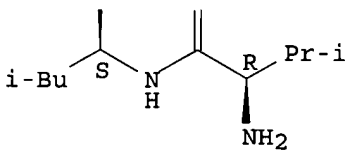

L9 ANSWER 3 OF 12 CAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 2002:637638 CAPLUS
DOCUMENT NUMBER: 137:185315

TITLE: Isophthalic acid derivatives as matrix **metalloproteinase** inhibitors, and their pharmaceutical compositions and use in the treatment of cancer, arthritis, and congestive heart failure.

INVENTOR(S): Barvian, Nicole Chantel; Connor, David Thomas; Dyer, Richard Dennis; Johnson, Adam Richard; Patt, William Chester

PATENT ASSIGNEE(S): Warner-Lambert Company, USA

SOURCE: PCT Int. Appl., 64 pp.
CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2002064547	A2	20020822	WO 2002-IB344	20020204
WO 2002064547	A3	20021205		

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM

RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

US 2002156061	A1	20021024	US 2002-75918	20020213

PRIORITY APPLN. INFO.: US 2001-268736P P 20010214

OTHER SOURCE(S): MARPAT 137:185315

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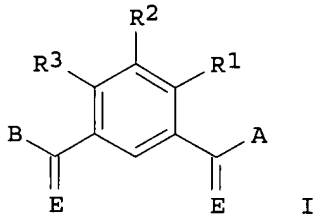

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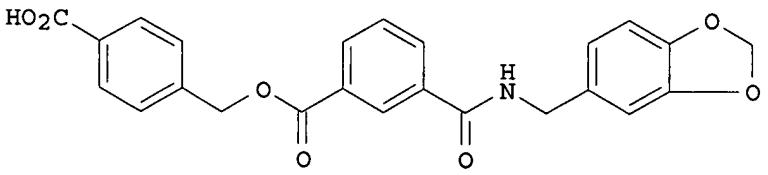


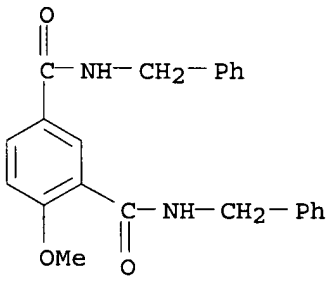
II

AB Selective MMP-13 inhibitors are disclosed, specifically isophthalic acid derivs. I or pharmaceutically acceptable salts thereof [wherein: R1, R2, R3 = H, halo, OH, C1-6 alkyl, C1-6 alkoxy, C2-6 alkenyl, C2-6 alkynyl, NO2, NR4R5, cyano, or CF3; E = O or S; A, B = OR4 or NR4R5; R4, R5 = H, C1-6 alkyl, C2-6 alkenyl, C2-6 alkynyl, (CH2)n-aryl, (CH2)n-cycloalkyl, (CH2)n-heteroaryl; or NR4R5 = (un)substituted 3- to 8-membered ring, optionally contg. an addnl. O, S, or NH; n = 0-6]. The compds. are useful for treating diseases in a mammal that are mediated by MMP enzymes. Specifically claimed uses are treatment of cancer, rheumatoid arthritis, osteoarthritis, and congestive heart failure. Approx. 70 compds. were prepd. and/or claimed. Some of the compds. were prepd.by a combinatorial

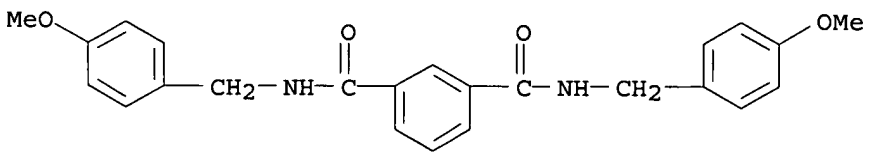
method. For instance, N-(1,3-benzodioxol-5-ylmethyl)isophthalamic acid was esterified with 4-(bromomethyl)benzoic acid tert-Bu ester using Cs2CO3 in DMF, and the resultant tert-Bu ester function was cleaved with TFA in anisole to give title compd. II. This compd. had IC50 (nM) values as follows: >100,000 for MMP-1; 30,000 for MMP-3; and 33 for MMP-13, thus showing high selectivity for the latter.

IT **143569-91-9P**, N,N'-Dibenzyl-4-methoxyisophthalamide
349396-68-5P, N,N'-Bis(4-methoxybenzyl)isophthalamide
383163-58-4P, N,N'-Bis-(1,3-benzodioxol-5-ylmethyl)isophthalamide
449790-17-4P, 4-Methoxy-N,N'-bis(4-methoxybenzyl)isophthalamide
449790-74-3P, N,N'-Bis-(1,3-benzodioxol-5-ylmethyl)-4-methoxyisophthalamide **449790-79-8P**, N-(1,3-Benzodioxol-5-ylmethyl)-4-methoxy-N'-(4-methoxybenzyl)isophthalamide **449790-84-5P**, N-(1,3-Benzodioxol-5-ylmethyl)-N'-(4-chlorobenzyl)-4-methoxyisophthalamide **449790-87-8P**, N-Benzyl-4-methoxy-N'-(4-methoxybenzyl)isophthalamide **449790-90-3P**, N'-Benzyl-4-methoxy-N-(4-methoxybenzyl)isophthalamide **449790-95-8P**, 4-Methoxy-N-(4-methoxybenzyl)-N'-pyridin-4-ylmethylisophthalamide **449791-12-2P**, N'-(1,3-Benzodioxol-5-ylmethyl)-4-methoxy-N-(2-phenoxyethyl)isophthalamide **449791-15-5P**, N-(1,3-Benzodioxol-5-ylmethyl)-4-methoxy-N'-(2-phenoxyethyl)isophthalamide **449791-18-8P**, N-(1,3-Benzodioxol-5-ylmethyl)-N'-furan-2-ylmethylisophthalamide **449791-20-2P**, N'-(1,3-Benzodioxol-5-ylmethyl)-N-(2-ethoxyethyl)-4-methoxyisophthalamide **449791-25-7P**, N,N'-Bis(3-hydroxymethylphenyl)isophthalamide **449791-28-0P**, N-Benzyl-4-methoxy-N'-(2-phenoxyethyl)isophthalamide **449791-31-5P**, 4-Methoxy-N,N'-bis(4-methylbenzyl)isophthalamide **449791-35-9P**, 4-Methoxy-N,N'-bis(3-methoxybenzyl)isophthalamide
RL: CPN (Combinatorial preparation); PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); CMBI (Combinatorial study); PREP (Preparation); USES (Uses)
(drug candidate; prepn. and use of isophthalic acid derivs. as selective MMP-13 inhibitors)

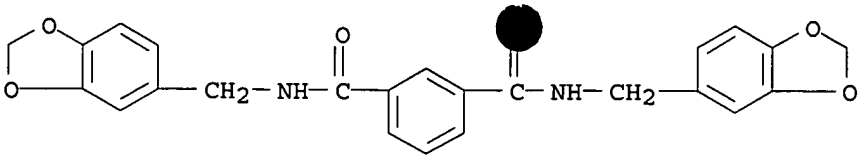
RN 143569-91-9 CAPLUS
CN 1,3-Benzenedicarboxamide, 4-methoxy-N,N'-bis(phenylmethyl)- (9CI) (CA INDEX NAME)



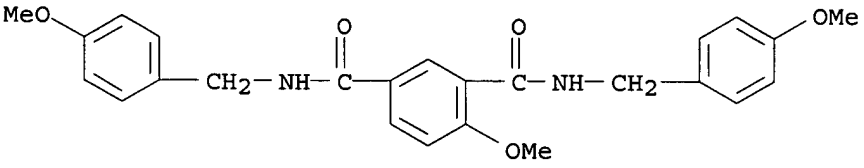
RN 349396-68-5 CAPLUS
CN 1,3-Benzenedicarboxamide, N,N'-bis[(4-methoxyphenyl)methyl]- (9CI) (CA INDEX NAME)



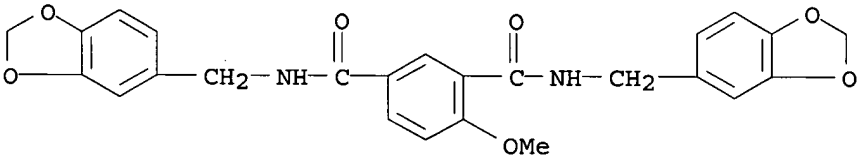
RN 383163-58-4 CAPLUS
CN 1,3-Benzenedicarboxamide, N,N'-bis(1,3-benzodioxol-5-ylmethyl)- (9CI) (CA INDEX NAME)



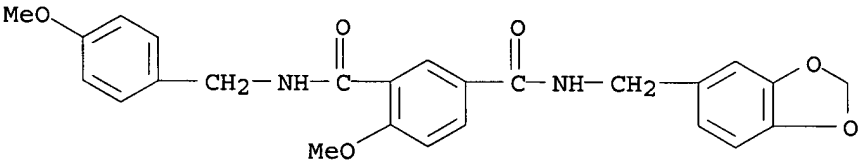
RN 449790-17-4 CAPLUS
CN 1,3-Benzenedicarboxamide, 4-methoxy-N,N'-bis[(4-methoxyphenyl)methyl]- (9CI) (CA INDEX NAME)



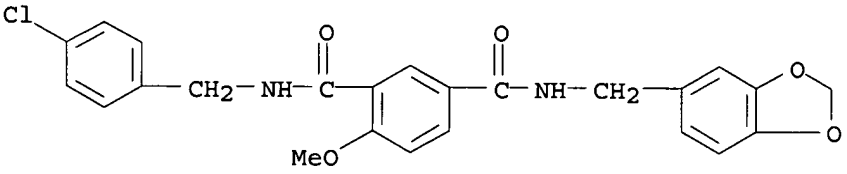
RN 449790-74-3 CAPLUS
CN 1,3-Benzenedicarboxamide, N,N'-bis(1,3-benzodioxol-5-ylmethyl)-4-methoxy- (9CI) (CA INDEX NAME)



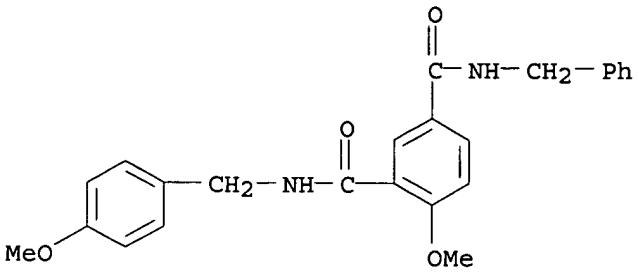
RN 449790-79-8 CAPLUS
CN 1,3-Benzenedicarboxamide, N1-(1,3-benzodioxol-5-ylmethyl)-4-methoxy-N3-[(4-methoxyphenyl)methyl]- (9CI) (CA INDEX NAME)



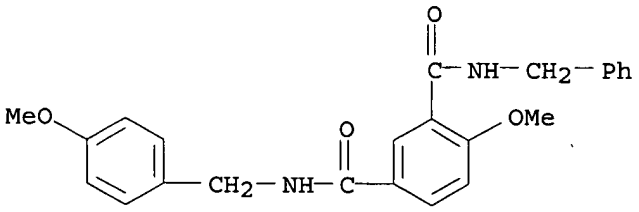
RN 449790-84-5 CAPLUS
CN 1,3-Benzenedicarboxamide, N1-(1,3-benzodioxol-5-ylmethyl)-N3-[(4-chlorophenyl)methyl]-4-methoxy- (9CI) (CA INDEX NAME)



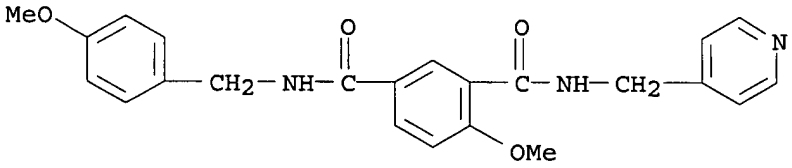
RN 449790-87-8 CAPLUS
CN 1,3-Benzenedicarboxamide, 4-methoxy-N3-[(4-methoxyphenyl)methyl]-N1-(phenylmethyl)- (9CI) (CA INDEX NAME)



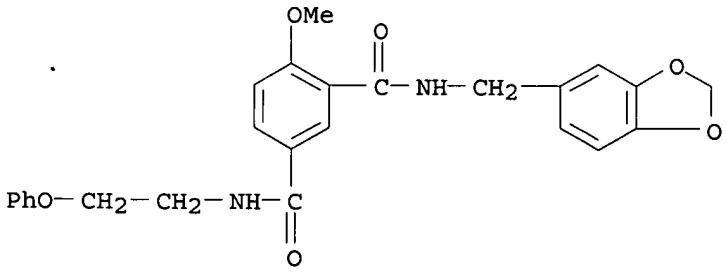
RN 449790-90-3 CAPLUS
CN 1,3-Benzenedicarboxamide, 4-methoxy-N1-[(4-methoxyphenyl)methyl]-N3-(phenylmethyl)- (9CI) (CA INDEX NAME)



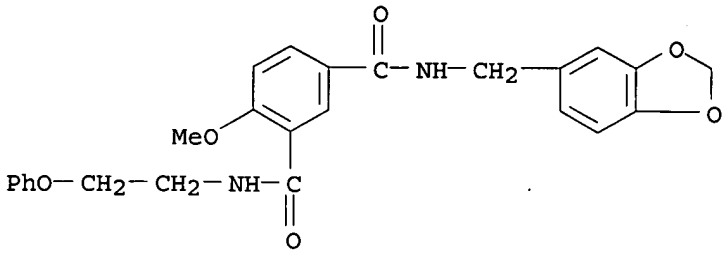
RN 449790-95-8 CAPLUS
CN 1,3-Benzenedicarboxamide, 4-methoxy-N1-[(4-methoxyphenyl)methyl]-N3-(4-pyridinylmethyl)- (9CI) (CA INDEX NAME)



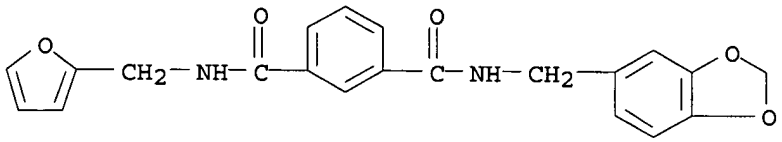
RN 449791-12-2 CAPLUS
CN 1,3-Benzenedicarboxamide, N3-(1,3-benzodioxol-5-ylmethyl)-4-methoxy-N1-(2-phenoxyethyl)- (9CI) (CA INDEX NAME)



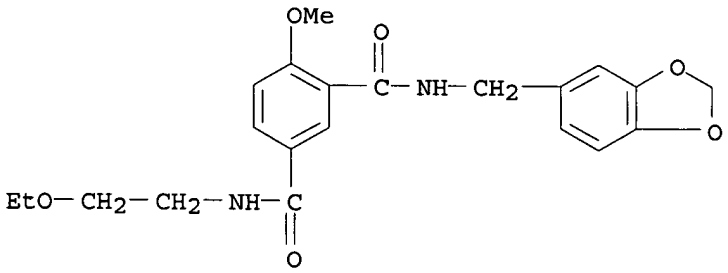
RN 449791-15-5 CAPLUS
CN 1,3-Benzenedicarboxamide, N1-(1,3-benzodioxol-5-ylmethyl)-4-methoxy-N3-(2-phenoxyethyl)- (9CI) (CA INDEX NAME)



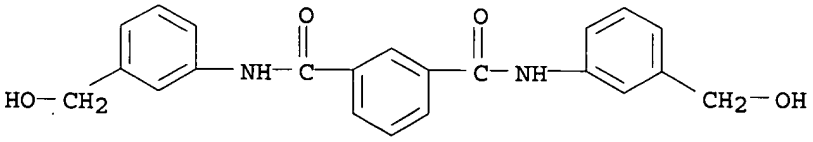
RN 449791-18-8 CAPLUS
CN 1,3-Benzenedicarboxamide, N-(1,3-benzodioxol-5-ylmethyl)-N'-(2-furanylmethyl)- (9CI) (CA INDEX NAME)



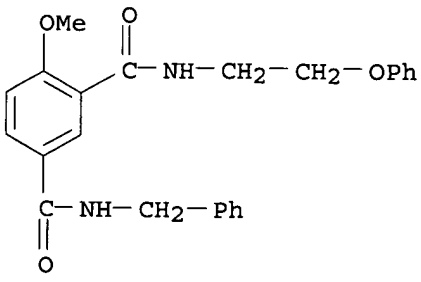
RN 449791-20-2 CAPLUS
CN 1,3-Benzenedicarboxamide, N3-(1,3-benzodioxol-5-ylmethyl)-N1-(2-ethoxyethyl)-4-methoxy- (9CI) (CA INDEX NAME)



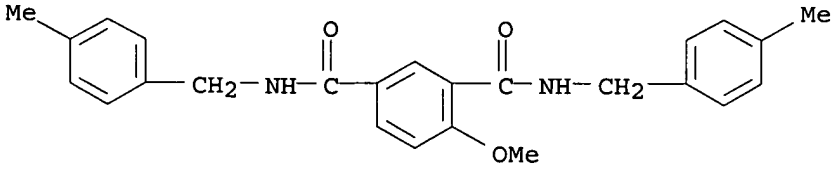
RN 449791-25-7 CAPLUS
CN 1,3-Benzenedicarboxamide, N,N'-bis[3-(hydroxymethyl)phenyl]- (9CI) (CA INDEX NAME)



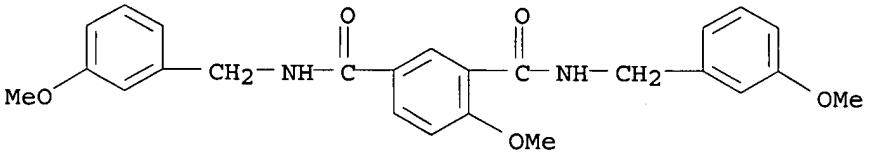
RN 449791-28-0 CAPLUS
CN 1,3-Benzenedicarboxamide, 4-methoxy-N3-(2-phenoxyethyl)-N1-(phenylmethyl)- (9CI) (CA INDEX NAME)



RN 449791-31-5 CAPLUS
CN 1,3-Benzenedicarboxamide, 4-methoxy-N,N'-bis[(4-methylphenyl)methyl]- (9CI) (CA INDEX NAME)

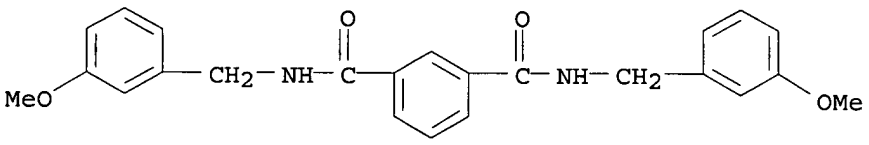


RN 449791-35-9 CAPLUS
CN 1,3-Benzenedicarboxamide, 4-methoxy-N,N'-bis[(3-methoxyphenyl)methyl]- (9CI) (CA INDEX NAME)

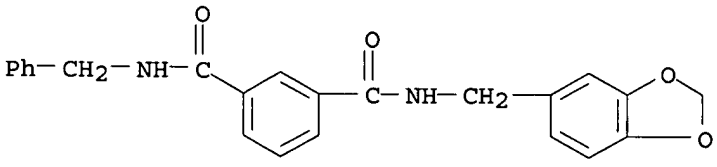


IT **449790-98-1P**, N,N'-Bis(3-methoxybenzyl)isophthalamide **449791-01-9P**, N-(1,3-Benzodioxol-5-ylmethyl)-N'-benzylisophthalamide **449791-04-2P**, N-(1,3-Benzodioxol-5-ylmethyl)-N'-(4-methoxybenzyl)isophthalamide **449791-09-7P**, N-Benzyl-N'-(4-methoxybenzyl)isophthalamide
RL: CPN (Combinatorial preparation); PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); CMBI (Combinatorial study); PREP (Preparation); USES (Uses)
(drug candidate; prepn. and use of isophthalic acid derivs. as selective MMP-13 inhibitors)

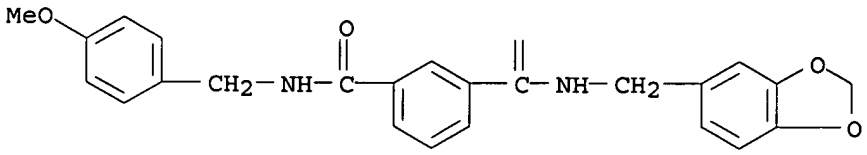
RN 449790-98-1 CAPLUS
CN 1,3-Benzenedicarboxamide, N,N'-bis[(3-methoxyphenyl)methyl]- (9CI) (CA INDEX NAME)



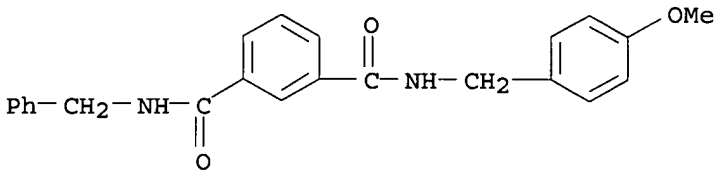
RN 449791-01-9 CAPLUS
CN 1,3-Benzenedicarboxamide, N-(1,3-benzodioxol-5-ylmethyl)-N'-(phenylmethyl)- (9CI) (CA INDEX NAME)



RN 449791-04-2 CAPLUS
CN 1,3-Benzenedicarboxamide, N-(1,3-benzodioxol-5-ylmethyl)-N'-[(4-methoxyphenyl)methyl]- (9CI) (CA INDEX NAME)

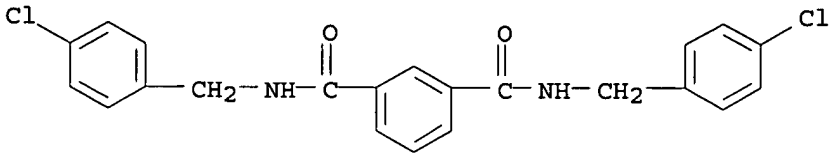


RN 449791-09-7 CAPLUS
CN 1,3-Benzenedicarboxamide, N-[(4-methoxyphenyl)methyl]-N'-(phenylmethyl)-(9CI) (CA INDEX NAME)

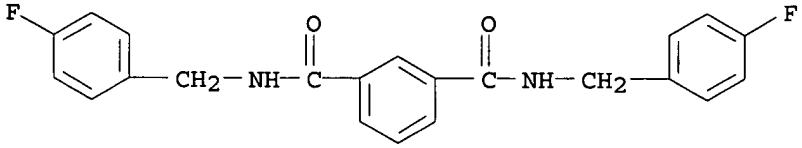


IT **449790-36-7P**, N,N'-Bis(4-chlorobenzyl)isophthalamide
449790-52-7P, N,N'-Bis(4-fluorobenzyl)isophthalamide
449790-57-2P, N,N'-Bis(3-fluorobenzyl)isophthalamide
449790-60-7P, N,N'-Bis(3-chlorobenzyl)isophthalamide
449791-38-2P, N'-(1,3-Benzodioxol-5-ylmethyl)-4-methoxy-N-(4-methoxybenzyl)isophthalamide **449791-41-7P**, 4-Amino-N,N'-bis-(1,3-benzodioxol-5-ylmethyl)isophthalamide **449791-44-0P**, 4-Acetylamino-N,N'-bis-(1,3-benzodioxol-5-ylmethyl)isophthalamide **449791-47-3P**, N-(3-Methoxybenzyl)-N'-pyridin-3-ylmethylisophthalamide **449791-50-8P**, N-(3-Methoxybenzyl)-N'-pyridin-4-ylmethylisophthalamide **449791-53-1P**, N-(1,3-Benzodioxol-5-ylmethyl)-N'-pyridin-3-ylmethylisophthalamide **449791-56-4P**, N-(4-Chlorobenzyl)-N'-(3-methoxybenzyl)isophthalamide **449791-59-7P**, N-(3,4-Dichlorobenzyl)-N'-(3-methoxybenzyl)isophthalamide **449791-62-2P**, N-(4-Methoxybenzyl)-N'-(3-methoxybenzyl)isophthalamide **449791-65-5P**, N-(3-Methoxybenzyl)-N'-(4-methylbenzyl)isophthalamide **449791-68-8P**, N,N'-Bis(4-fluoro-3-methoxybenzyl)isophthalamide **449791-71-3P**, [[3-[(1,3-Benzodioxol-5-ylmethyl)carbamoyl]benzoyl]benzylamino]acetic acid **449791-77-9P**, N-(3,4-Dichlorobenzyl)-N'-pyridin-4-ylmethylisophthalamide **449791-81-5P**, N-(3-Methoxybenzyl)-N'-(4-nitrobenzyl)isophthalamide **449791-84-8P**, 4-[[3-(3-Methoxybenzylcarbamoyl)benzoylamino]methyl]benzoic acid methyl ester **449791-90-6P**, 4-[[3-(3-Methoxybenzylcarbamoyl)benzoylamino]methyl]benzoic acid **449791-93-9P**, N-(3-Aminobenzyl)-N'-(3-methoxybenzyl)isophthalamide **449791-96-2P**, N-(3-Methoxybenzyl)-N'-(3-nitrobenzyl)isophthalamide **449791-99-5P**, 4-Ethoxy-N,N'-bis(3-methoxybenzyl)isophthalamide **449792-02-3P**, N,N'-Bis-(1,3-Benzodioxol-5-ylmethyl)-4-ethoxyisophthalamide **449792-04-5P**, N,N'-Bis-(1,3-Benzodioxol-5-ylmethyl)-4-propoxyisophthalamide **449792-07-8P**, N,N'-Bis-(1,3-benzodioxol-5-ylmethyl)-4-isopropoxyisophthalamide **449792-10-3P**, N,N'-Bis-(2,1,3-benzothiadiazol-5-ylmethyl)-4-methoxyisophthalamide **449792-16-9P**, N-(3-Methoxybenzyl)-N'-(3-trifluoromethoxybenzyl)isophthalamide **449792-18-1P**, 4-Isopropoxy-N,N'-bis(3-methoxybenzyl)isophthalamide
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(drug candidate; prepn. and use of isophthalic acid derivs. as selective MMP-13 inhibitors)

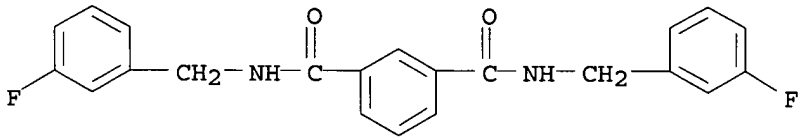
RN 449790-36-7 CAPLUS
CN 1,3-Benzenedicarboxamide, N,N'-bis[(4-chlorophenyl)methyl]- (9CI) (CA INDEX NAME)



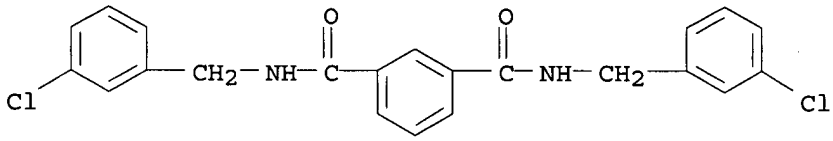
RN 449790-52-7 CAPLUS
CN 1,3-Benzenedicarboxamide, N,N'-bis[(4-fluorophenyl)methyl]- (9CI) (CA INDEX NAME)



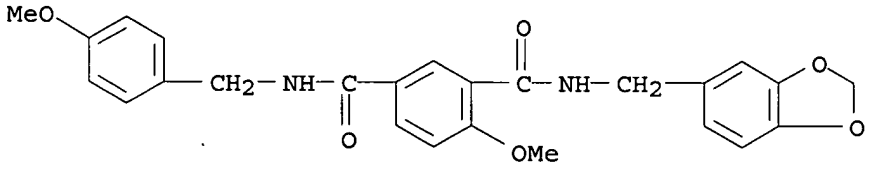
RN 449790-57-2 CAPLUS
CN 1,3-Benzenedicarboxamide, N,N'-bis[(3-fluorophenyl)methyl]- (9CI) (CA INDEX NAME)



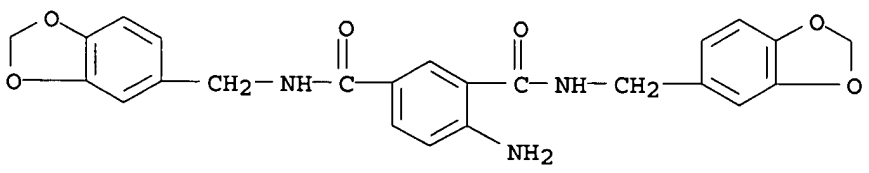
RN 449790-60-7 CAPLUS
CN 1,3-Benzenedicarboxamide, N,N'-bis[(3-chlorophenyl)methyl]- (9CI) (CA INDEX NAME)



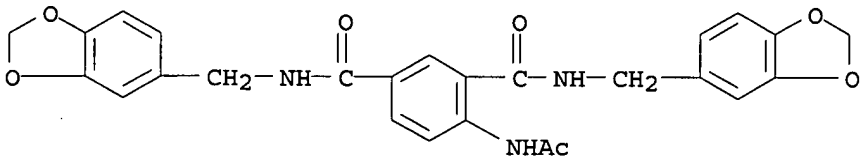
RN 449791-38-2 CAPLUS
CN 1,3-Benzenedicarboxamide, N3-(1,3-benzodioxol-5-ylmethyl)-4-methoxy-N1-[(4-methoxyphenyl)methyl]- (9CI) (CA INDEX NAME)



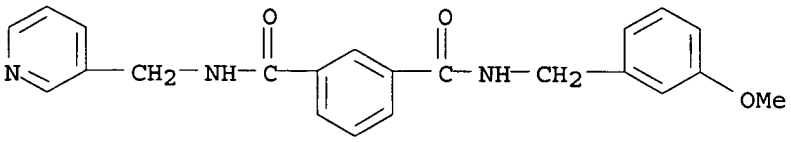
RN 449791-41-7 CAPLUS
CN 1,3-Benzenedicarboxamide, 4-amino-N,N'-bis(1,3-benzodioxol-5-ylmethyl)- (9CI) (CA INDEX NAME)



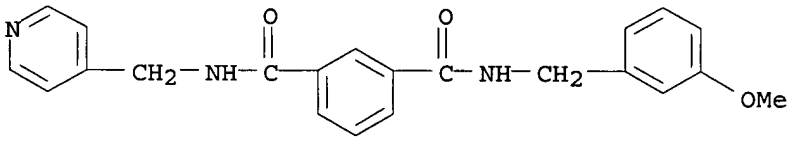
RN 449791-44-0 CAPLUS
CN 1,3-Benzenedicarboxamide, 4-(acetylamino)-N,N'-bis(1,3-benzodioxol-5-ylmethyl)- (9CI) (CA INDEX NAME)



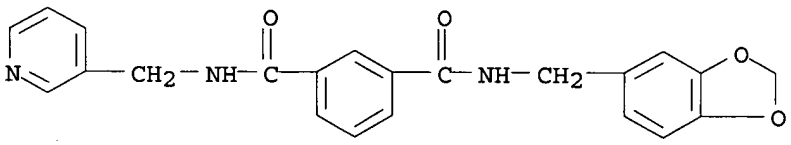
RN 449791-47-3 CAPLUS
CN 1,3-Benzenedicarboxamide, N-[(3-methoxyphenyl)methyl]-N'-(3-pyridinylmethyl)- (9CI) (CA INDEX NAME)



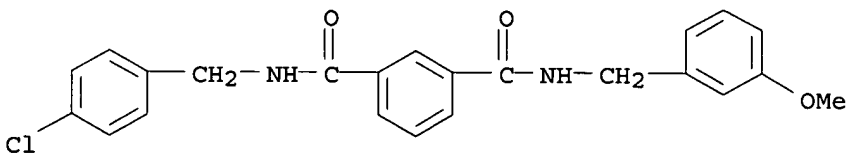
RN 449791-50-8 CAPLUS
CN 1,3-Benzenedicarboxamide, N-[(3-methoxyphenyl)methyl]-N'-(4-pyridinylmethyl)- (9CI) (CA INDEX NAME)



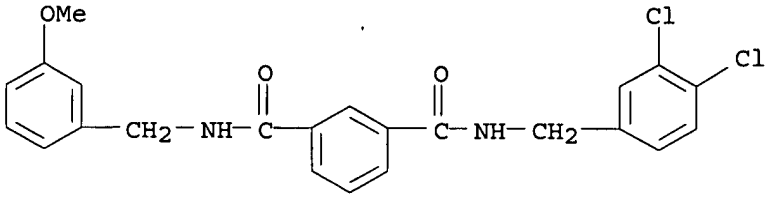
RN 449791-53-1 CAPLUS
CN 1,3-Benzenedicarboxamide, N-(1,3-benzodioxol-5-ylmethyl)-N'-(3-pyridinylmethyl)- (9CI) (CA INDEX NAME)



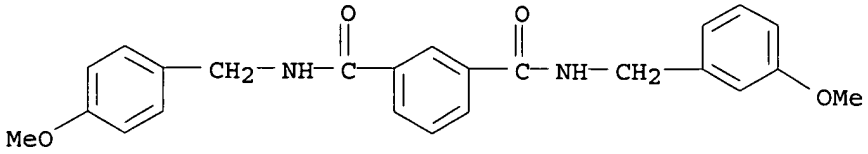
RN 449791-56-4 CAPLUS
CN 1,3-Benzenedicarboxamide, N-[(4-chlorophenyl)methyl]-N'-[(3-methoxyphenyl)methyl]- (9CI) (CA INDEX NAME)



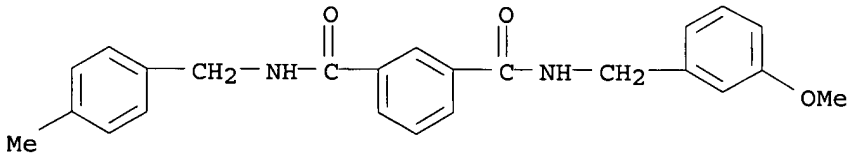
RN 449791-59-7 CAPLUS
CN 1,3-Benzenedicarboxamide, N-[(3,4-dichlorophenyl)methyl]-N'-[(3-methoxyphenyl)methyl]- (9CI) (CA INDEX NAME)



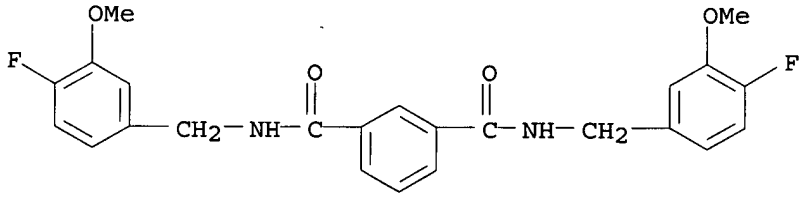
RN 449791-62-2 CAPLUS
CN 1,3-Benzenedicarboxamide, N-[(3-methoxyphenyl)methyl]-N'-[(4-methoxyphenyl)methyl]- (9CI) (CA INDEX NAME)



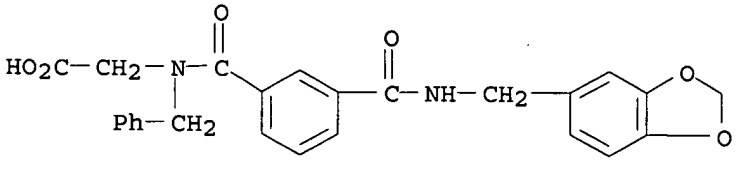
RN 449791-65-5 CAPLUS
CN 1,3-Benzenedicarboxamide, N-[(3-methoxyphenyl)methyl]-N'-[(4-methylphenyl)methyl]- (9CI) (CA INDEX NAME)



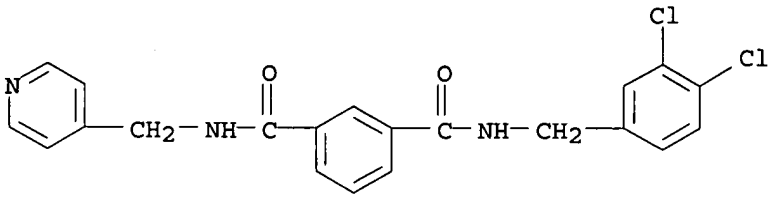
RN 449791-68-8 CAPLUS
CN 1,3-Benzenedicarboxamide, N,N'-bis[(4-fluoro-3-methoxyphenyl)methyl]- (9CI) (CA INDEX NAME)



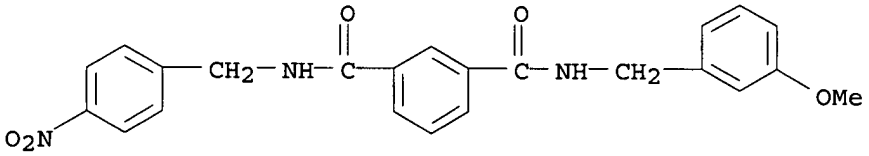
RN 449791-71-3 CAPLUS
CN Glycine, N-[3-[[(1,3-benzodioxol-5-ylmethyl)amino]carbonyl]benzoyl]-N-(phenylmethyl)- (9CI) (CA INDEX NAME)



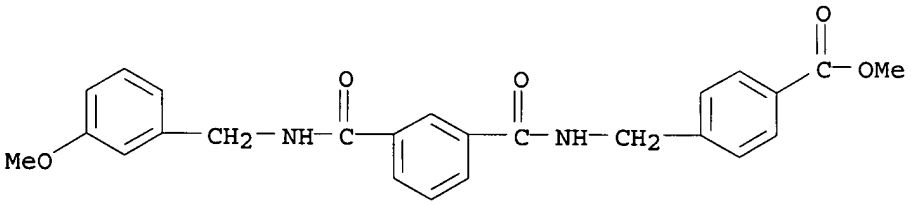
RN 449791-77-9 CAPLUS
CN 1,3-Benzenedicarboxamide, N-[(3,4-dichlorophenyl)methyl]-N'-(4-pyridinylmethyl)- (9CI) (CA INDEX NAME)



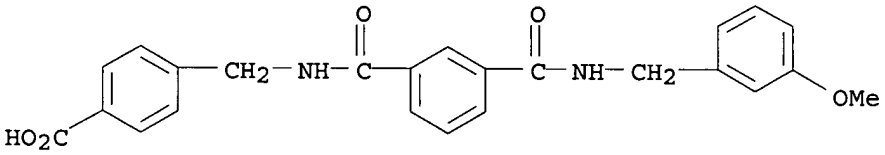
RN 449791-81-5 CAPLUS
CN 1,3-Benzenedicarboxamide, N-[(3-methoxyphenyl)methyl]-N'-[(4-nitrophenyl)methyl]- (9CI) (CA INDEX NAME)



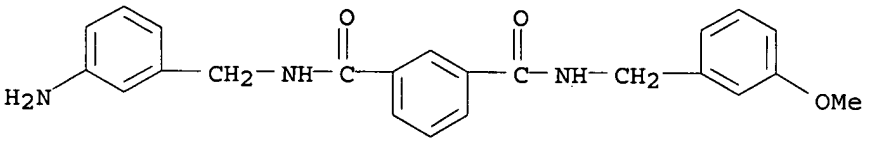
RN 449791-84-8 CAPLUS
CN Benzoic acid, 4-[[[3-[[[(3-methoxyphenyl)methyl]amino]carbonyl]benzoyl]amino]methyl]-, methyl ester (9CI) (CA INDEX NAME)



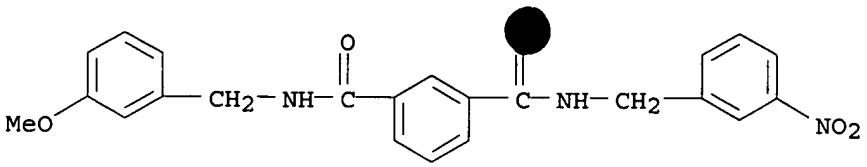
RN 449791-90-6 CAPLUS
CN Benzoic acid, 4-[[[3-[[[(3-methoxyphenyl)methyl]amino]carbonyl]benzoyl]amino]methyl]- (9CI) (CA INDEX NAME)



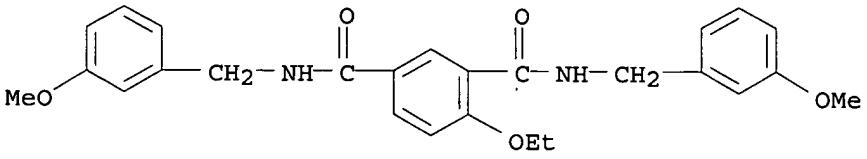
RN 449791-93-9 CAPLUS
CN 1,3-Benzenedicarboxamide, N-[(3-aminophenyl)methyl]-N'-[(3-methoxyphenyl)methyl]- (9CI) (CA INDEX NAME)



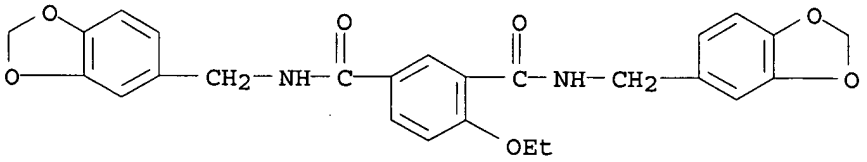
RN 449791-96-2 CAPLUS
CN 1,3-Benzenedicarboxamide, N-[(3-methoxyphenyl)methyl]-N'-[(3-nitrophenyl)methyl]- (9CI) (CA INDEX NAME)



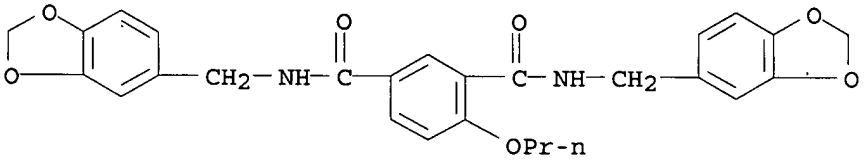
RN 449791-99-5 CAPLUS
CN 1,3-Benzenedicarboxamide, 4-ethoxy-N,N'-bis[(3-methoxyphenyl)methyl]- (9CI) (CA INDEX NAME)



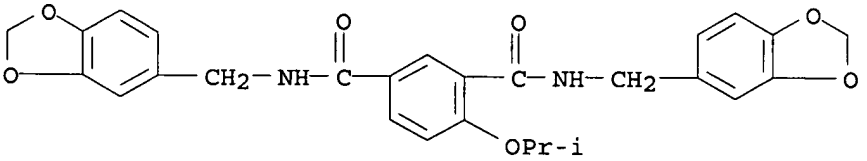
RN 449792-02-3 CAPLUS
CN 1,3-Benzenedicarboxamide, N,N'-bis(1,3-benzodioxol-5-ylmethyl)-4-ethoxy- (9CI) (CA INDEX NAME)



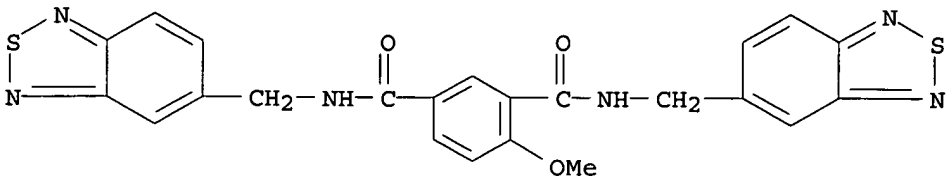
RN 449792-04-5 CAPLUS
CN 1,3-Benzenedicarboxamide, N,N'-bis(1,3-benzodioxol-5-ylmethyl)-4-propoxy- (9CI) (CA INDEX NAME)



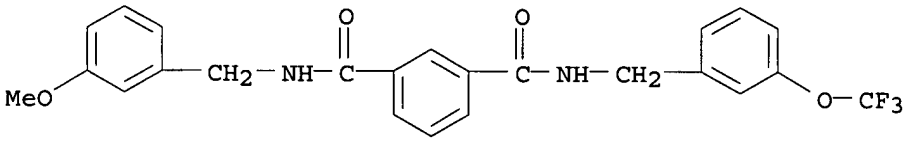
RN 449792-07-8 CAPLUS
CN 1,3-Benzenedicarboxamide, N,N'-bis(1,3-benzodioxol-5-ylmethyl)-4-(1-methylethoxy)- (9CI) (CA INDEX NAME)



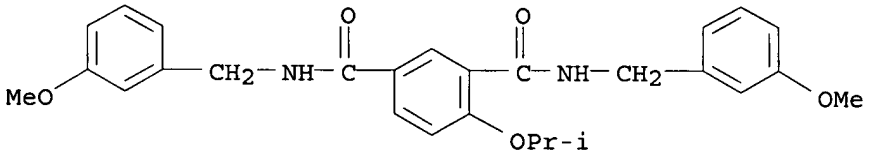
RN 449792-10-3 CAPLUS
CN 1,3-Benzenedicarboxamide, N,N'-bis(2,1,3-benzothiadiazol-5-ylmethyl)-4-methoxy- (9CI) (CA INDEX NAME)



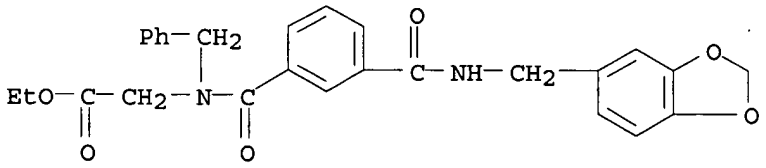
RN 449792-16-9 CAPLUS
CN 1,3-Benzenedicarboxamide, N-[(3-methoxyphenyl)methyl]-N'-[[3-(trifluoromethoxy)phenyl]methyl]- (9CI) (CA INDEX NAME)



RN 449792-18-1 CAPLUS
CN 1,3-Benzenedicarboxamide, N,N'-bis[(3-methoxyphenyl)methyl]-4-(1-methylethoxy)- (9CI) (CA INDEX NAME)



IT **449792-24-9P**, [[3-[(1,3-Benzodioxol-5-ylmethyl)carbamoyl]benzoyl]benzylamino]acetic acid ethyl ester
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(intermediate; prepn. and use of isophthalic acid derivs. as selective MMP-13 inhibitors)
RN 449792-24-9 CAPLUS
CN Glycine, N-[3-[[(1,3-benzodioxol-5-ylmethyl)amino]carbonyl]benzoyl]-N-(phenylmethyl)-, ethyl ester (9CI) (CA INDEX NAME)



L9 ANSWER 4 OF 12 CAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 2002:637472 CAPLUS
DOCUMENT NUMBER: 137:201321
TITLE: Preparation of substituted isophthalic acid derivatives, multicyclic pyrimidinediones and analogs thereof as matrix **metalloproteinase** inhibitors
INVENTOR(S): Andrianjara, Charles; Ortwine, Daniel Fred; Pavlovsky, Alexander Gregory; Roark, William Howard
PATENT ASSIGNEE(S): Warner-Lambert Company, USA
SOURCE: PCT Int. Appl., 173 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2002064080	A2	20020822	WO 2002-IB447	20020213
WO 2002064080	A3	20021212		

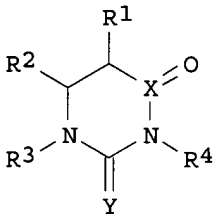
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM

RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

US 2003078276	A1	20030424	US 2002-75069	20020213

PRIORITY APPLN. INFO.: US 2001-268821P P 20010214

GI



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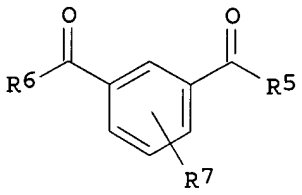

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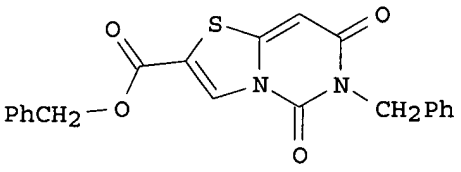


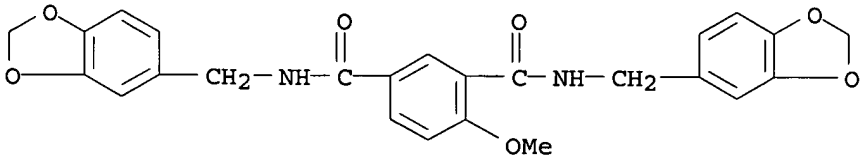
III

AB Title compds., I [R1 and R2 together may form a substituted arom. ring or a heterocyclic ring; or R2 and R3 together may form substituted heterocycle; or R1, R3, or R4 = alkyl, arylalkyl, etc.; X = C, S; Y = O, N with provision when Y = N it forms a 5-membered heterocycle with R3] and II [R5, R6 = arylalkylamine, heterocyclylalkoxy, etc.; R7 = H, MeO, NO2, etc.], are prepd. and disclosed as matrix **metalloproteinase** (MMP) inhibitors. Thus, III was prepd. in five steps via cyclocondensation of diethylmalonate and benzylurea with subsequent chlorination, substitution with hydrosulfide hydrate to form an in situ intermediate that was reacted with bromoacetaldehyde dimethylacetal, followed by acid catalyzed cyclization and substitution with benzylchloroformate. III was demonstrated to inhibit MMP13 with an IC50 value (in .mu.M) of 0.0230. I and II bind allosterically to the catalytic domain of MMP-13 and comprise a hydrophobic group, first and second hydrogen bond acceptors and at least one, and preferably both, of a third hydrogen bond acceptor and a second hydrophobic group. Cartesian coordinates for centroids of the above features are defined in the specification. When the ligand binds to MMP-13, the first, second and third (when present) hydrogen bond acceptors bond resp. with Thr245, Thr247 and Met 253, the first hydrophobic group locates within the S1' channel of MMP-13 and the second hydrophobic group (when present) is relatively open to solvent. The compds. specifically inhibit the matrix **metalloproteinase**-13 enzyme and thus are useful for treating diseases resulting from tissue breakdown, such as heart disease, multiple sclerosis, arthritis, atherosclerosis, and osteoporosis.

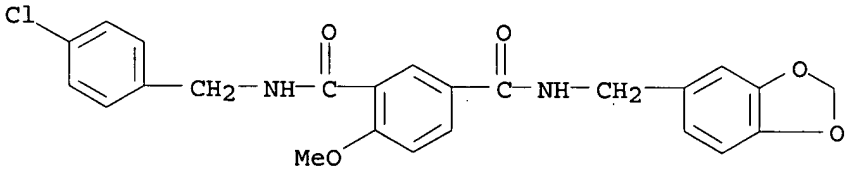
IT **449790-74-3P 449790-84-5P 449790-90-3P**

449791-35-9P
RL: CPN (Combinatorial preparation); PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); CMBI (Combinatorial study); PREP (Preparation); USES (Uses)
(combinatorial prepn. and pharmaceutical activity of substituted isophthalic acid derivs. as matrix **metalloproteinase** inhibitors)

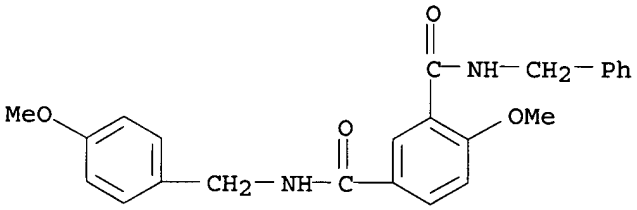
RN 449790-74-3 CAPLUS
CN 1,3-Benzenedicarboxamide, N,N'-bis(1,3-benzodioxol-5-ylmethyl)-4-methoxy- (9CI) (CA INDEX NAME)



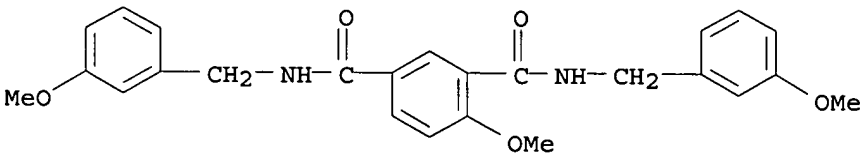
RN 449790-84-5 CAPLUS
CN 1,3-Benzenedicarboxamide, N1-(1,3-benzodioxol-5-ylmethyl)-N3-[(4-chlorophenyl)methyl]-4-methoxy- (9CI) (CA INDEX NAME)



RN 449790-90-3 CAPLUS
CN 1,3-Benzenedicarboxamide, 4-methoxy-N1-[(4-methoxyphenyl)methyl]-N3-(phenylmethyl)- (9CI) (CA INDEX NAME)



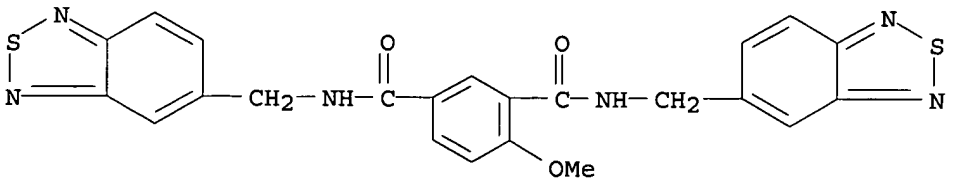
RN 449791-35-9 CAPLUS
CN 1,3-Benzenedicarboxamide, 4-methoxy-N,N'-bis[(3-methoxyphenyl)methyl]- (9CI) (CA INDEX NAME)



IT **449792-10-3P**
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(prepn. and pharmaceutical activity of substituted isophthalic acid derivs., multicyclic pyrimidinediones and analogs thereof as matrix **metalloproteinase** inhibitors)

RN 449792-10-3 CAPLUS

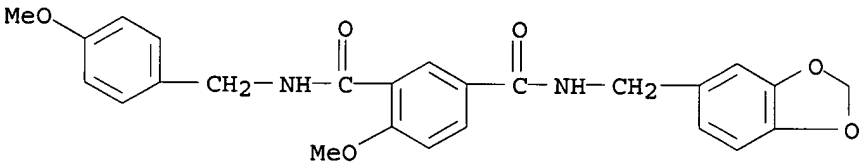
CN 1,3-Benzenedicarboxamide, [redacted]N'-bis(2,1,3-benzothiadiazol-5-[redacted]ethyl)-4-methoxy- (9CI) (CA INDEX NAME)



IT **449790-79-8P**
RL: CPN (Combinatorial preparation); PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); CMBI (Combinatorial study); PREP (Preparation); USES (Uses)
(target compd.; combinatorial prepn. and pharmaceutical activity of substituted isophthalic acid derivs. as matrix **metalloproteinase** inhibitors)

RN 449790-79-8 CAPLUS

CN 1,3-Benzenedicarboxamide, N1-(1,3-benzodioxol-5-ylmethyl)-4-methoxy-N3-[(4-methoxyphenyl)methyl]- (9CI) (CA INDEX NAME)



IT **143569-91-9P 349396-68-5P 383163-58-4P**
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449790-57-2P 449790-60-7P 449790-87-8P
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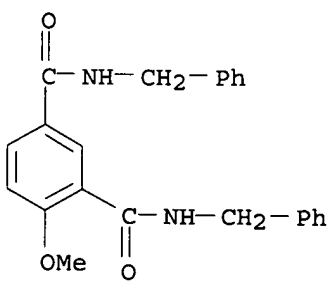
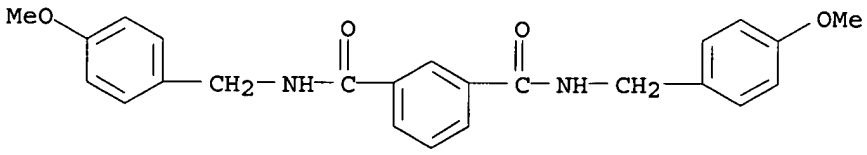
449791-53-1P 449791-56-4P 449791-59-7P
449791-62-2P 449791-65-5P 449791-68-8P
449791-71-3P 449791-77-9P 449791-81-5P
449791-84-8P 449791-90-6P 449791-93-9P
449791-96-2P 449791-99-5P 449792-02-3P
449792-04-5P 449792-07-8P 451471-35-5P
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(target compd.; prepn. and pharmaceutical activity of substituted isophthalic acid derivs., multicyclic pyrimidinediones and analogs thereof as matrix **metalloproteinase** inhibitors)

RN 143569-91-9 CAPLUS

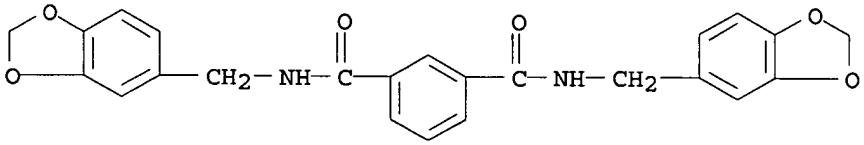
CN 1,3-Benzenedicarboxamide, 4-methoxy-N,N'-bis(phenylmethyl)- (9CI) (CA INDEX NAME)



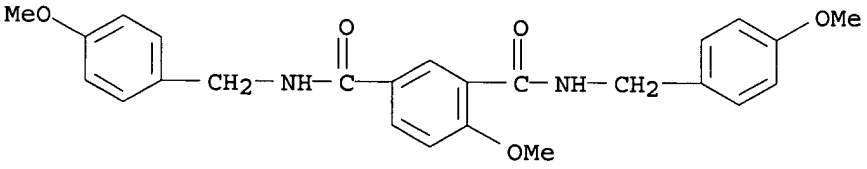
RN 349396-68-5 CAPLUS
CN 1,3-Benzenedicarboxamide, N,N'-bis[(4-methoxyphenyl)methyl]- (9CI) (CA INDEX NAME)



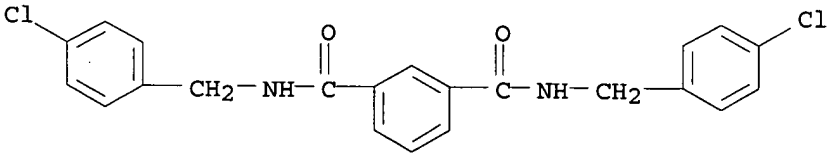
RN 383163-58-4 CAPLUS
CN 1,3-Benzenedicarboxamide, N,N'-bis(1,3-benzodioxol-5-ylmethyl)- (9CI) (CA INDEX NAME)



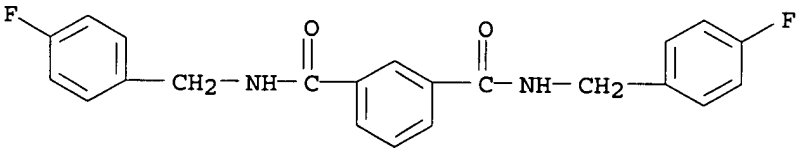
RN 449790-17-4 CAPLUS
CN 1,3-Benzenedicarboxamide, 4-methoxy-N,N'-bis[(4-methoxyphenyl)methyl]- (9CI) (CA INDEX NAME)



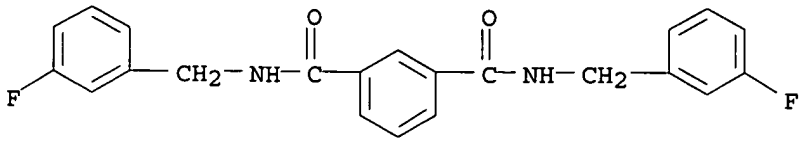
RN 449790-36-7 CAPLUS
CN 1,3-Benzenedicarboxamide, N,N'-bis[(4-chlorophenyl)methyl]- (9CI) (CA INDEX NAME)



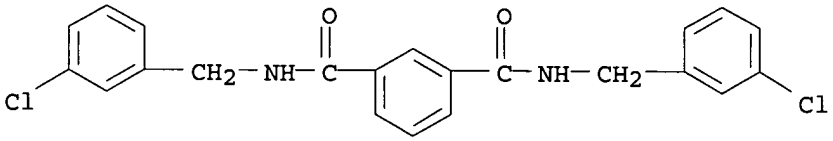
RN 449790-52-7 CAPLUS
CN 1,3-Benzenedicarboxamide, N,N'-bis[(4-fluorophenyl)methyl]- (9CI) (CA INDEX NAME)



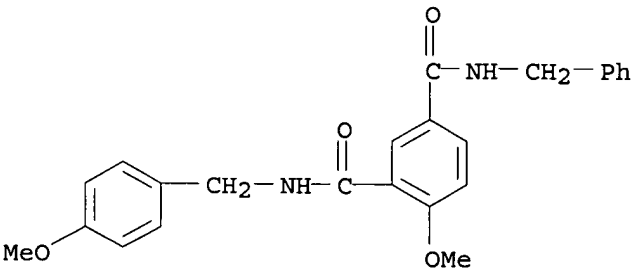
RN 449790-57-2 CAPLUS
CN 1,3-Benzenedicarboxamide, N,N'-bis[(3-fluorophenyl)methyl]- (9CI) (CA INDEX NAME)



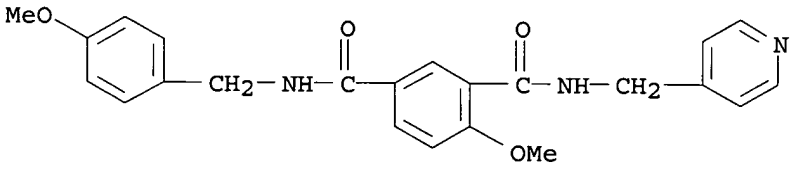
RN 449790-60-7 CAPLUS
CN 1,3-Benzenedicarboxamide, N,N'-bis[(3-chlorophenyl)methyl]- (9CI) (CA INDEX NAME)



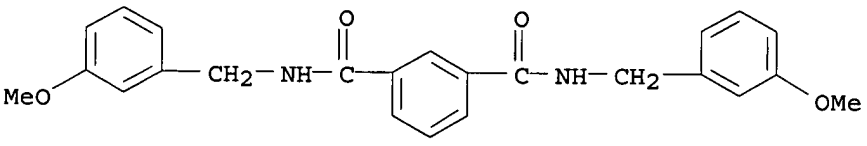
RN 449790-87-8 CAPLUS
CN 1,3-Benzenedicarboxamide, 4-methoxy-N3-[(4-methoxyphenyl)methyl]-N1-(phenylmethyl)- (9CI) (CA INDEX NAME)



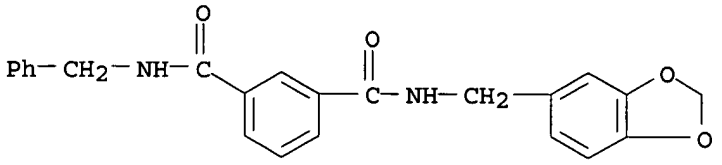
RN 449790-95-8 CAPLUS
CN 1,3-Benzenedicarboxamide, 4-methoxy-N1-[(4-methoxyphenyl)methyl]-N3-(4-pyridinylmethyl)- (9CI) (CA INDEX NAME)



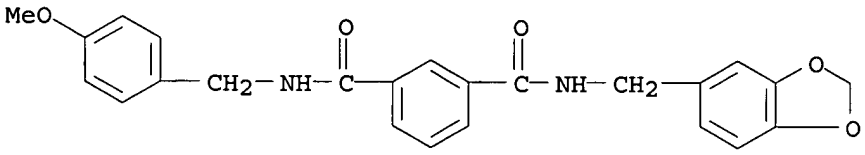
RN 449790-98-1 CAPLUS
CN 1,3-Benzenedicarboxamide, N,N'-bis[(3-methoxyphenyl)methyl]- (9CI) (CA INDEX NAME)



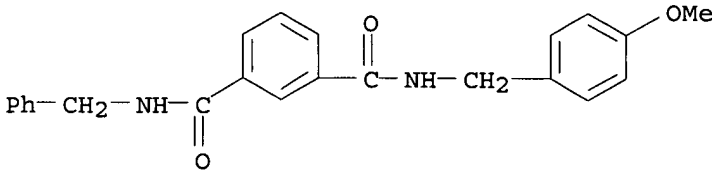
RN 449791-01-9 CAPLUS
CN 1,3-Benzenedicarboxamide, N-(1,3-benzodioxol-5-ylmethyl)-N'-(phenylmethyl)- (9CI) (CA INDEX NAME)



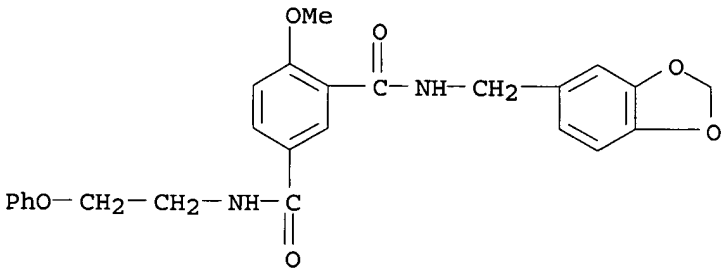
RN 449791-04-2 CAPLUS
CN 1,3-Benzenedicarboxamide, N-(1,3-benzodioxol-5-ylmethyl)-N'-[(4-methoxyphenyl)methyl]- (9CI) (CA INDEX NAME)



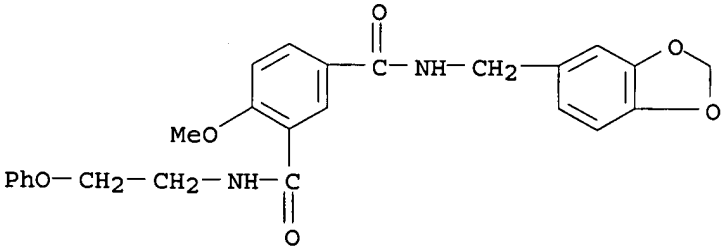
RN 449791-09-7 CAPLUS
CN 1,3-Benzenedicarboxamide, N-[(4-methoxyphenyl)methyl]-N'-(phenylmethyl)- (9CI) (CA INDEX NAME)



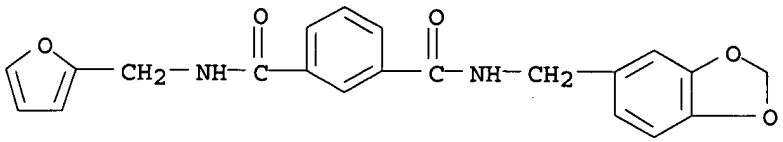
RN 449791-12-2 CAPLUS
CN 1,3-Benzenedicarboxamide, N3-(1,3-benzodioxol-5-ylmethyl)-4-methoxy-N1-(2-phenoxyethyl)- (9CI) (CA INDEX NAME)



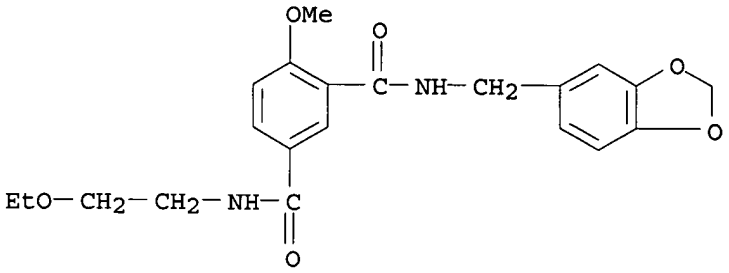
RN 449791-15-5 CAPLUS
CN 1,3-Benzenedicarboxamide, N1-(1,3-benzodioxol-5-ylmethyl)-4-methoxy-N3-(2-phenoxyethyl)- (9CI) (CA INDEX NAME)



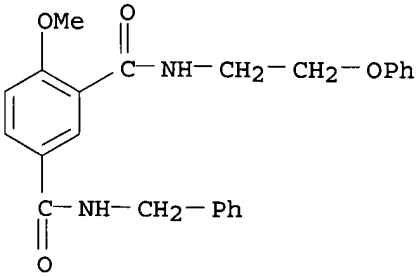
RN 449791-18-8 CAPLUS
CN 1,3-Benzenedicarboxamide, N-(1,3-benzodioxol-5-ylmethyl)-N'-(2-furanylmethyl)- (9CI) (CA INDEX NAME)



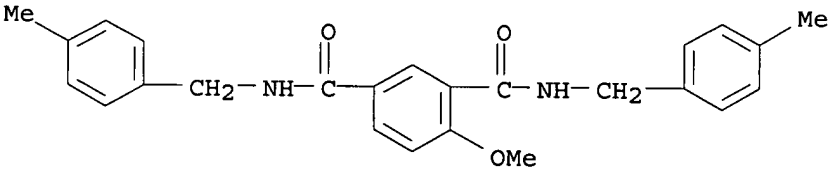
RN 449791-20-2 CAPLUS
CN 1,3-Benzenedicarboxamide, N3-(1,3-benzodioxol-5-ylmethyl)-N1-(2-ethoxyethyl)-4-methoxy- (9CI) (CA INDEX NAME)



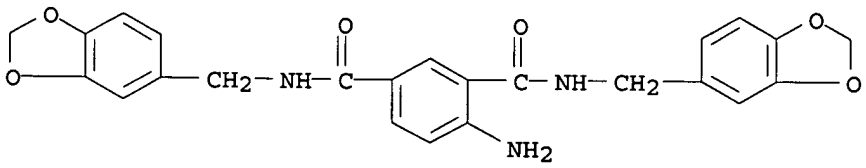
RN 449791-28-0 CAPLUS
CN 1,3-Benzenedicarboxamide, 4-methoxy-N3-(2-phenoxyethyl)-N1-(phenylmethyl)-(9CI) (CA INDEX NAME)



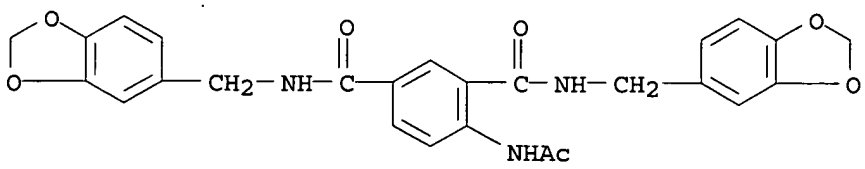
RN 449791-31-5 CAPLUS
CN 1,3-Benzenedicarboxamide, 4-methoxy-N,N'-bis[(4-methylphenyl)methyl]-(9CI) (CA INDEX NAME)



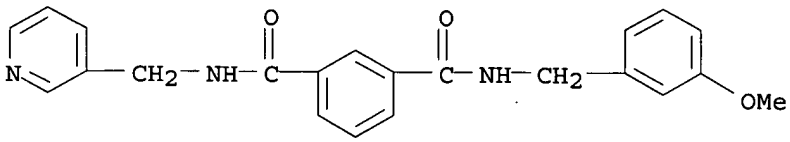
RN 449791-41-7 CAPLUS
CN 1,3-Benzenedicarboxamide, 4-amino-N,N'-bis(1,3-benzodioxol-5-ylmethyl)-(9CI) (CA INDEX NAME)



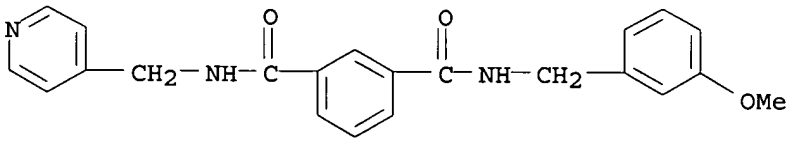
RN 449791-44-0 CAPLUS
CN 1,3-Benzenedicarboxamide, (acetylamino)-N,N'-bis(1,3-benzodioxol-5-ylmethyl)- (9CI) (CA INDEX NAME)



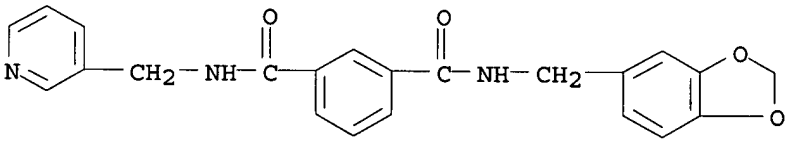
RN 449791-47-3 CAPLUS
CN 1,3-Benzenedicarboxamide, N-[(3-methoxyphenyl)methyl]-N'-(3-pyridinylmethyl)- (9CI) (CA INDEX NAME)



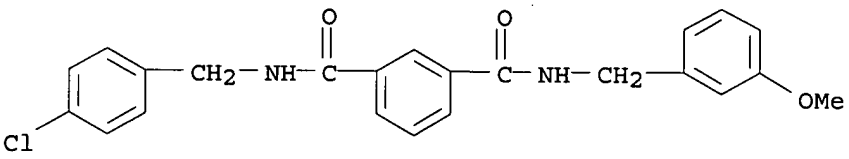
RN 449791-50-8 CAPLUS
CN 1,3-Benzenedicarboxamide, N-[(3-methoxyphenyl)methyl]-N'-(4-pyridinylmethyl)- (9CI) (CA INDEX NAME)



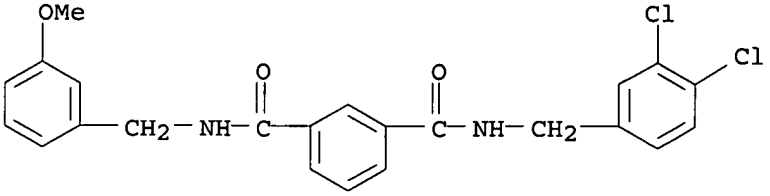
RN 449791-53-1 CAPLUS
CN 1,3-Benzenedicarboxamide, N-(1,3-benzodioxol-5-ylmethyl)-N'-(3-pyridinylmethyl)- (9CI) (CA INDEX NAME)



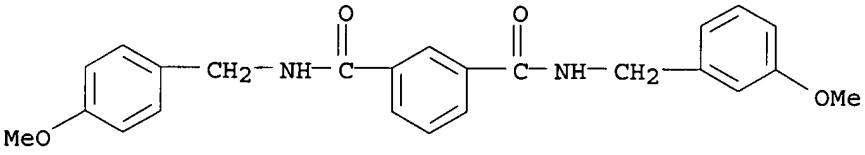
RN 449791-56-4 CAPLUS
CN 1,3-Benzenedicarboxamide, N-[(4-chlorophenyl)methyl]-N'-[(3-methoxyphenyl)methyl]- (9CI) (CA INDEX NAME)



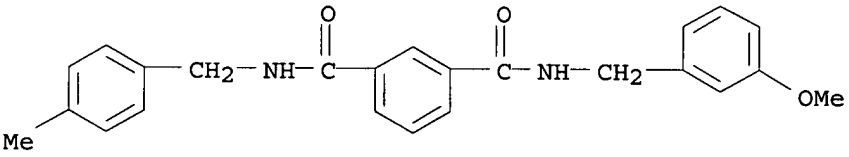
RN 449791-59-7 CAPLUS
CN 1,3-Benzenedicarboxamide, N-[(3,4-dichlorophenyl)methyl]-N'-[(3-methoxyphenyl)methyl]- (9CI) (CA INDEX NAME)



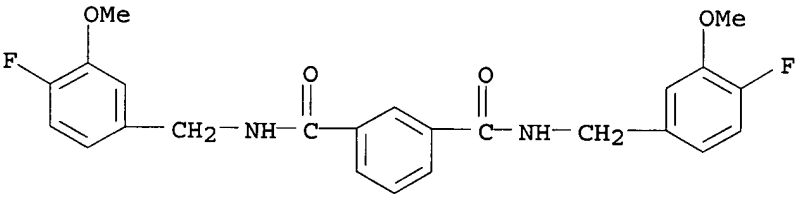
RN 449791-62-2 CAPLUS
CN 1,3-Benzenedicarboxamide, N-[(3-methoxyphenyl)methyl]-N'-[(4-methoxyphenyl)methyl]- (9CI) (CA INDEX NAME)



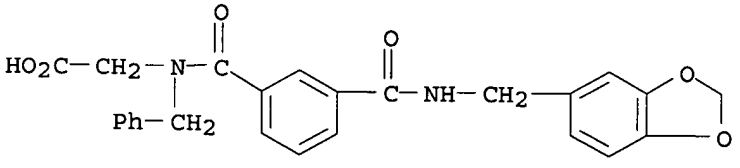
RN 449791-65-5 CAPLUS
CN 1,3-Benzenedicarboxamide, N-[(3-methoxyphenyl)methyl]-N'-[(4-methylphenyl)methyl]- (9CI) (CA INDEX NAME)



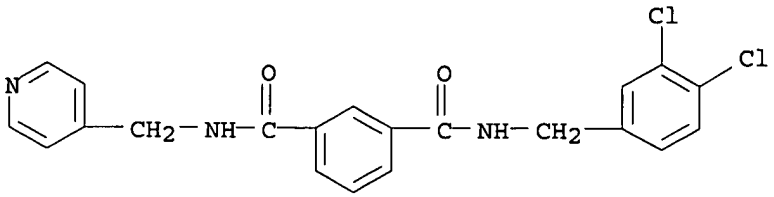
RN 449791-68-8 CAPLUS
CN 1,3-Benzenedicarboxamide, N,N'-bis[(4-fluoro-3-methoxyphenyl)methyl]- (9CI) (CA INDEX NAME)



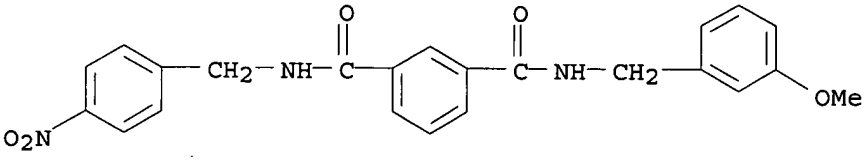
RN 449791-71-3 CAPLUS
CN Glycine, N-[3-[[(1,3-benzodioxol-5-ylmethyl)amino]carbonyl]benzoyl]-N-(phenylmethyl)- (9CI) (CA INDEX NAME)



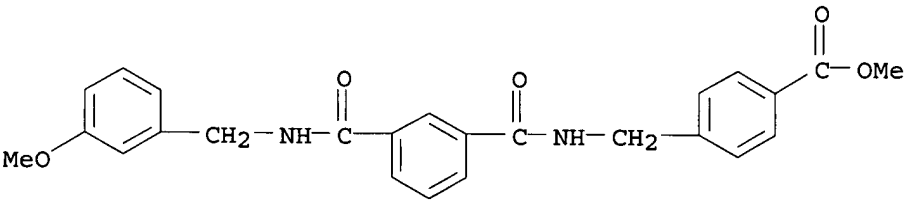
RN 449791-77-9 CAPLUS
CN 1,3-Benzenedicarboxamide, N-[(3,4-dichlorophenyl)methyl]-N'-(4-pyridinylmethyl)- (9CI) (CA INDEX NAME)



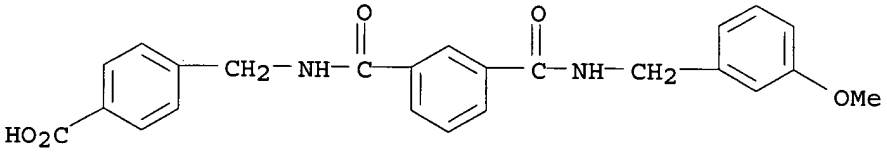
RN 449791-81-5 CAPLUS
CN 1,3-Benzenedicarboxamide, N-[(3-methoxyphenyl)methyl]-N'-[(4-nitrophenyl)methyl]- (9CI) (CA INDEX NAME)



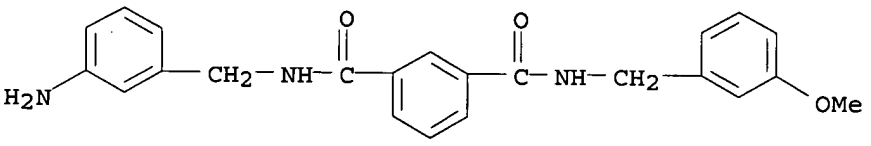
RN 449791-84-8 CAPLUS
CN Benzoic acid, 4-[[[3-[[[(3-methoxyphenyl)methyl]amino]carbonyl]benzoyl]amino]methyl]-, methyl ester (9CI) (CA INDEX NAME)



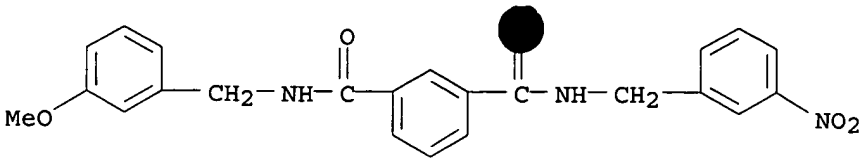
RN 449791-90-6 CAPLUS
CN Benzoic acid, 4-[[[3-[[[(3-methoxyphenyl)methyl]amino]carbonyl]benzoyl]amino]methyl]- (9CI) (CA INDEX NAME)



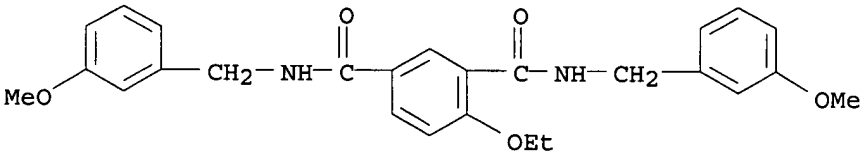
RN 449791-93-9 CAPLUS
CN 1,3-Benzenedicarboxamide, N-[(3-aminophenyl)methyl]-N'-[(3-methoxyphenyl)methyl]- (9CI) (CA INDEX NAME)



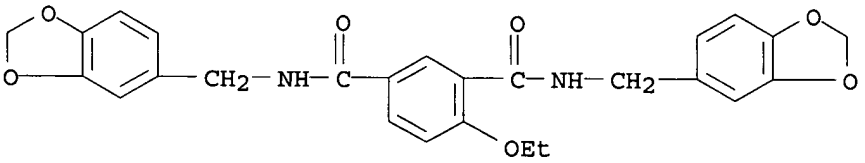
RN 449791-96-2 CAPLUS
CN 1,3-Benzenedicarboxamide, N-[(3-methoxyphenyl)methyl]-N'-[(3-nitrophenyl)methyl]- (9CI) (CA INDEX NAME)



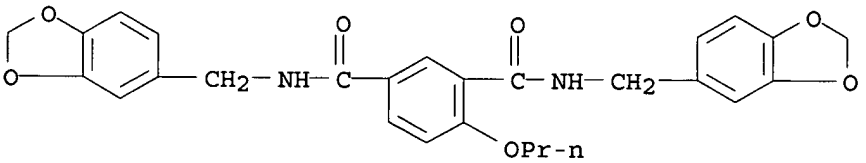
RN 449791-99-5 CAPLUS
CN 1,3-Benzenedicarboxamide, 4-ethoxy-N,N'-bis[(3-methoxyphenyl)methyl]- (9CI) (CA INDEX NAME)



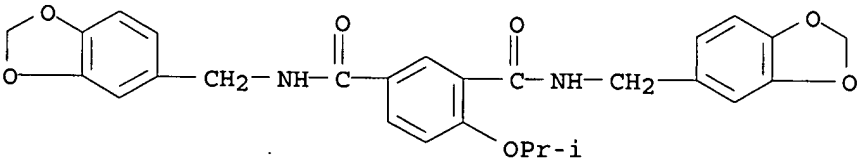
RN 449792-02-3 CAPLUS
CN 1,3-Benzenedicarboxamide, N,N'-bis(1,3-benzodioxol-5-ylmethyl)-4-ethoxy- (9CI) (CA INDEX NAME)



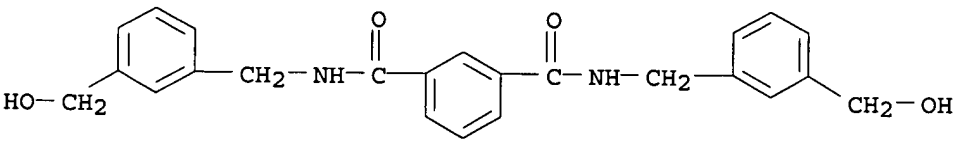
RN 449792-04-5 CAPLUS
CN 1,3-Benzenedicarboxamide, N,N'-bis(1,3-benzodioxol-5-ylmethyl)-4-propoxy- (9CI) (CA INDEX NAME)

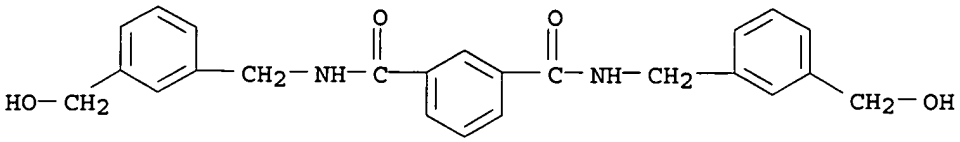


RN 449792-07-8 CAPLUS
CN 1,3-Benzenedicarboxamide, N,N'-bis(1,3-benzodioxol-5-ylmethyl)-4-(1-methylethoxy)- (9CI) (CA INDEX NAME)



RN 451471-35-5 CAPLUS
CN 1,3-Benzenedicarboxamide, N,N'-bis[[3-(hydroxymethyl)phenyl]methyl]- (9CI) (CA INDEX NAME)



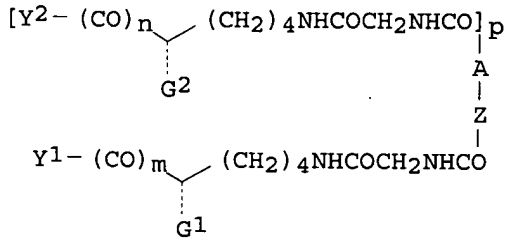


L9 ANSWER 5 OF 12 CAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 2001:730694 CAPLUS
DOCUMENT NUMBER: 135:273223
TITLE: Preparation of glycyllysine derivatives for inhibition of angiogenesis and tumor growth
INVENTOR(S): Boger, Dale L.; Cheresh, David A.
PATENT ASSIGNEE(S): Scripps Research Institute, USA
SOURCE: PCT Int. Appl., 59 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001072699	A1	20011004	WO 2001-US9756	20010327
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
EP 1276713	A1	20030122	EP 2001-924359	20010327
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR				
JP 2003528850	T2	20030930	JP 2001-570612	20010327
NO 2002004578	A	20021120	NO 2002-4578	20020924
US 2003083519	A1	20030501	US 2002-240141	20020927

PRIORITY APPLN. INFO.: US 2000-192260P P 20000327
WO 2001-US9756 W 20010327

OTHER SOURCE(S): MARPAT 135:273223
GI



I

AB Compds. I [G1, G2 = NHCO2R1 (R1 = alkyl), Q-(CH2)vC6H4-X1 (Q = NHCO2, NHCONH, O2CNH, OCO2; X1 = halo, nitro, alkyl, alkoxy, perfluoroalkyl; v = 1 or 2), or NHCOCH2C6H4X1; Y1, Y2 = OH, alkyl, hydroxyalkyl, alkoxy, Ph, benzyl or NH2; Z = C.tplbond.C, C6H4, cis- or trans-CH:CH, -CH2CH:CHCH2, -1,3- or 1,4-cyclohexyl, or 1,4-naphthyl; A is H or a covalent bond; m, n = 0 or 1 (with provisos)] which inhibit tumor growth and angiogenesis are provided. These compds. include glycyllysine derivs. bound to a central arom. linking core. Thus, N,N'-isophthaloylbis[N6-glycyl-N2-[[[4-(trifluoromethyl)phenyl]methoxy]carbonyl]-L-lysine] was prepd. from p-trifluoromethylbenzyl alc. by reaction with disuccinimidyl carbonate, coupling with N.vepsiln.-(tert-butoxycarbonyl)lysine Me ester,

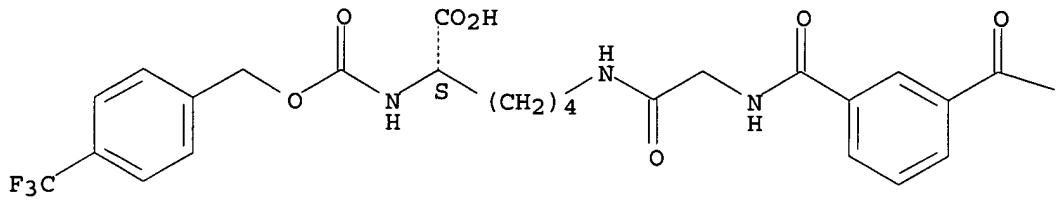
deprotection, condensation with isophthaloyl dichloride, and [redacted]apon.

IT **331678-22-9P 331714-17-1P 362709-20-4P**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(prepn. of glycyllysine derivs. for inhibition of angiogenesis and tumor growth)

RN 331678-22-9 CAPLUS
CN L-Lysine, N6,N6'-[1,3-phenylenebis[carbonylimino(1-oxo-2,1-ethanediyl)]]bis[N2-[[[4-(trifluoromethyl)phenyl]methoxy]carbonyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



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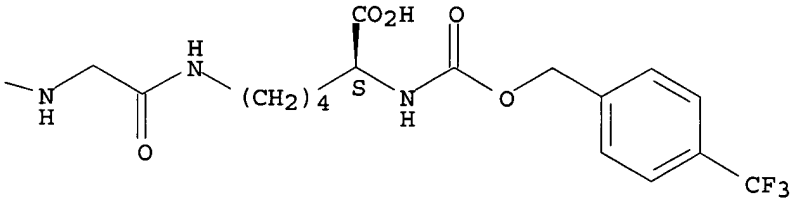
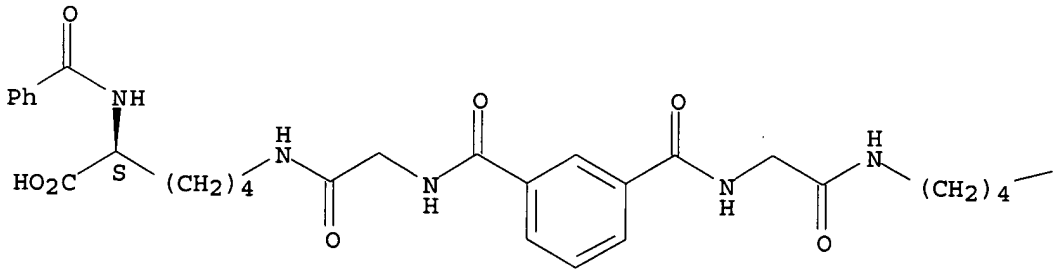


RN 331714-17-1 CAPLUS
CN L-Lysine, N6,N6'-[1,3-phenylenebis[carbonylimino(1-oxo-2,1-ethanediyl)]]bis[N2-benzoyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



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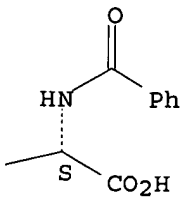
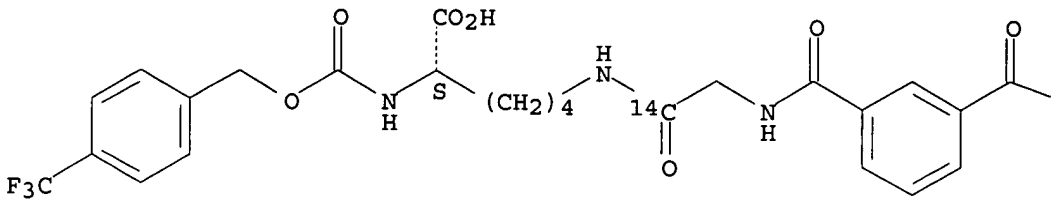


RN 362709-20-4 CAPLUS

CN L-Lysine, N6,N6'-[1,3-phenylenebis[carbonylimino(1-oxo-2,1-ethanediyl-1-14C)]]bis[N2-[[[4-(trifluoromethyl)phenyl]methoxy]carbonyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



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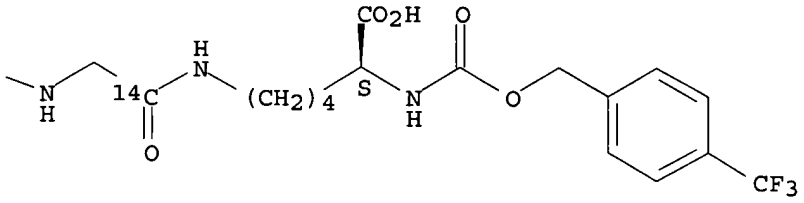


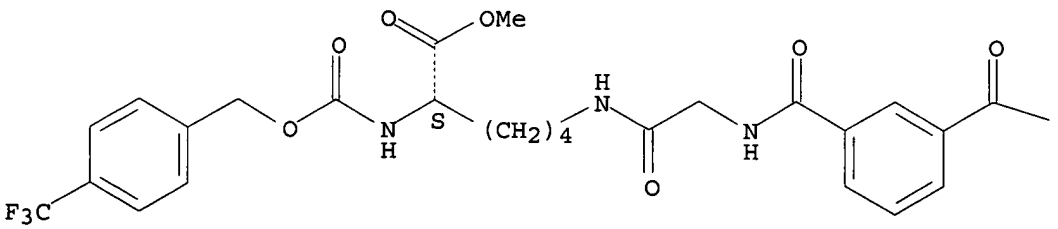
IT **331714-10-4P 331714-16-0P 362709-18-0P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(prepn. of glycyllysine derivs. for inhibition of angiogenesis and tumor growth)

RN 331714-10-4 CAPLUS

CN L-Lysine, N6,N6'-[1,3-phenylenebis[carbonylimino(1-oxo-2,1-ethanediyl)]]bis[N2-[[[4-(trifluoromethyl)phenyl]methoxy]carbonyl]-, dimethyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



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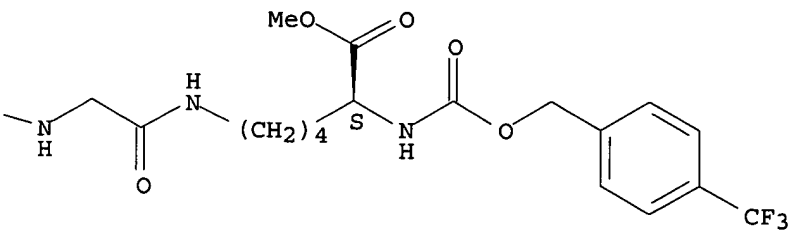
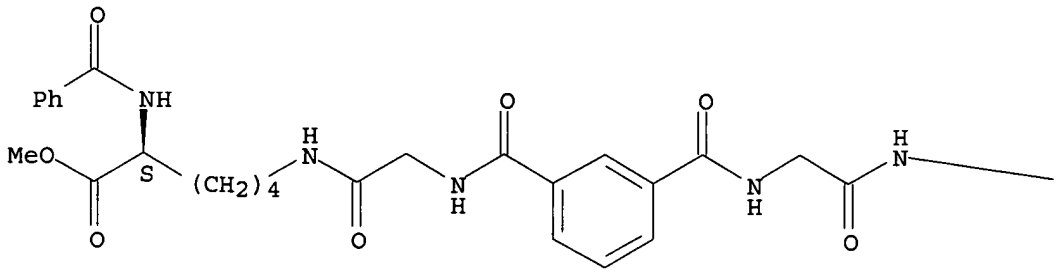


RN 331714-16-0 CAPLUS

CN L-Lysine, N6,N6'-[1,3-phenylenebis[carbonylimino(1-oxo-2,1-ethanediyl)]]bis[N2-benzoyl-, dimethyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



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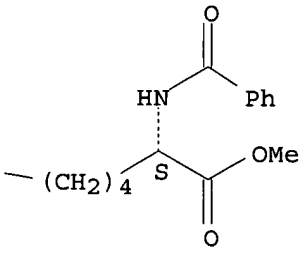
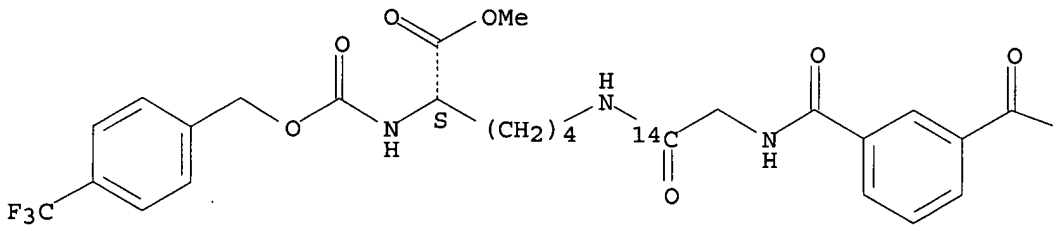


RN 362709-18-0 CAPLUS
CN L-Lysine, N6,N6'-[1,3-phenylenebis[carbonylimino(1-oxo-2,1-ethanediyl-1-14C)]]bis[N2-[[[4-(trifluoromethyl)phenyl]methoxy]carbonyl]-, dimethyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



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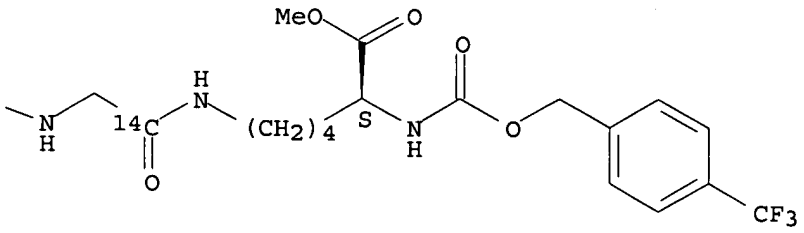

REFERENCE COUNT: 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L9 ANSWER 6 OF 12 CAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 2001:730544 CAPLUS
DOCUMENT NUMBER: 135:289058
TITLE: Preparation of glycyllysine derivatives for inhibition of angiogenesis and tumor growth

INVENTOR(S): Boger, [redacted]le L.; Cheresh, David A.
PATENT ASSIGNEE(S): The Scripps Research Institute, USA
SOURCE: PCT Int. Appl., 41 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001072297	A1	20011004	WO 2001-US9785	20010327
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
EP 1272173	A1	20030108	EP 2001-922734	20010327
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR				
JP 2003528140	T2	20030924	JP 2001-570258	20010327
NO 2002004576	A	20021120	NO 2002-4576	20020924
US 2003078296	A1	20030424	US 2002-240142	20020927

PRIORITY APPLN. INFO.: US 2000-192260P P 20000327
WO 2001-US9785 W 20010327
OTHER SOURCE(S): MARPAT 135:289058
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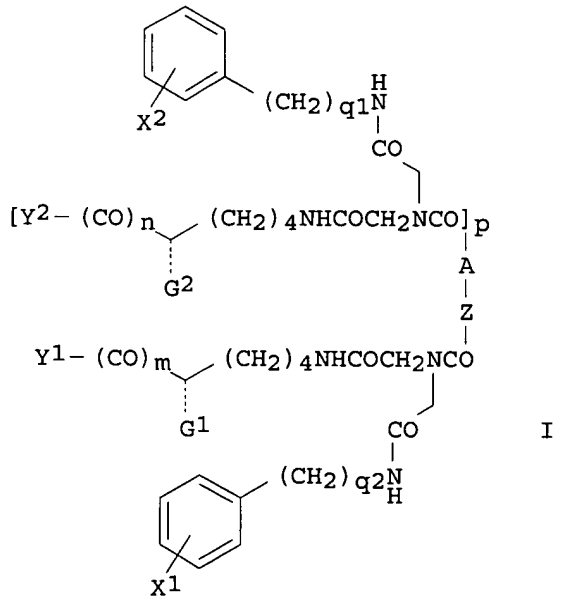


AB Compds. I [G1, G2 = NHCO2R1 (R1 = alkyl), Q-(CH2)vC6H4-X3 (Q = NHCO2, NHCONH, O2CNH, OCO2; X3 = halo, nitro, alkyl, alkoxy, perfluoroalkyl; v = 1 or 2), or NHCOCH2C6H4X3; Y1, Y2 = OH, alkyl, hydroxyalkyl, alkoxy, Ph, benzyl or NH2; X1, X2 = halo, alkoxy; Z = C.tplbond.C, C6H4, cis- or trans-CH:CH, -CH2CH:CHCH2, -1,3- or 1,4-cyclohexyl, or 1,4-naphthyl; A is H or a covalent bond; m, n, p = 0 or 1; Q1, Q2 = 1 or 2 (with provisos)] which inhibit tumor growth and angiogenesis are provided. These compds. include glycyllysine derivs. bound to a central arom. linking core. Thus, N,N'-isophthaloylbis[N6-[N-[2-[(4-fluorophenethyl)amino]-2-oxoethyl]glycyl]-N2-[[[4-(trifluoromethyl)phenyl]methoxy]carbonyl]-L-lysine] di-Me ester was prepd. from p-trifluoromethylbenzyl alc. by reaction with disuccinimidyl carbonate, coupling N.epsilon.-Boc-Lys-OMe,

(Boc = tert-butoxycarbonyl and BocN(CH2CO2H)CH2CONHCH2CH2C F-4, deprotection, and condensation with isophthaloyl dichloride.

IT **331714-00-2P**

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)

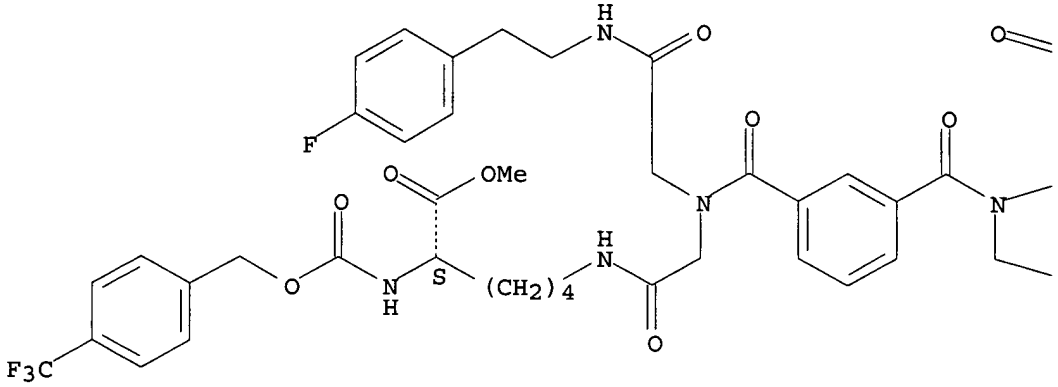
(prepn. of glycyllysine derivs. for inhibition of angiogenesis and tumor growth)

RN 331714-00-2 CAPLUS

CN L-Lysine, 1,1'-(1,3-phenylenedicarbonyl)bis[N6-[N-[2-[[2-(4-fluorophenyl)ethyl]amino]-2-oxoethyl]glycyl]-N2-[[[4-(trifluoromethyl)phenyl]methoxy]carbonyl]-, dimethyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



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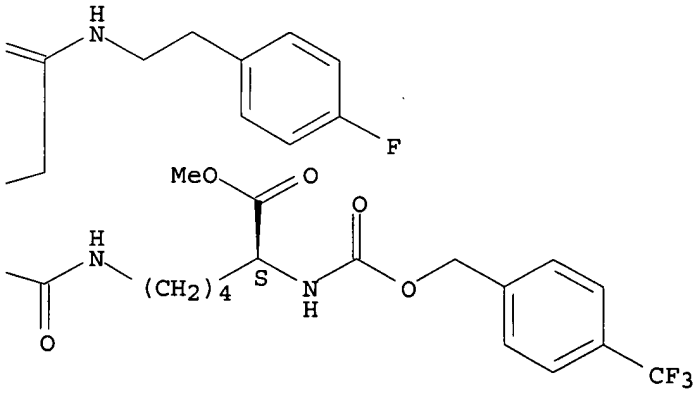


IT **215161-86-7P 215161-90-3P 215161-92-5P**
215161-93-6P 215161-94-7P 215161-95-8P
215161-99-2P 331713-91-8P 331713-92-9P
331713-93-0P 331713-94-1P 331713-95-2P
331713-96-3P 331713-98-5P 331713-99-6P
331714-01-3P 331714-02-4P 331714-03-5P
364361-95-5P 364362-02-7P 364362-05-0P
364362-08-3P

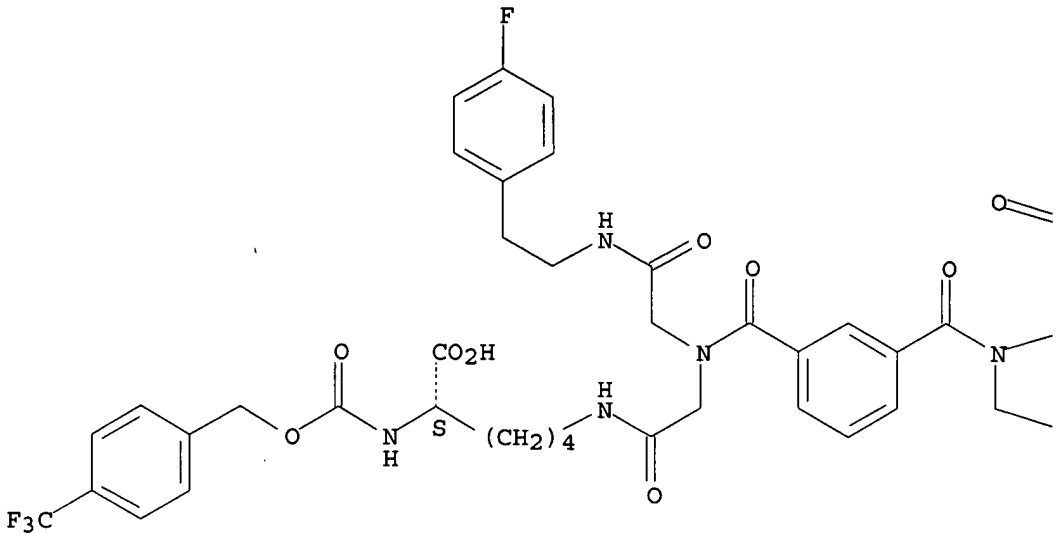
L9 ANSWER 7 OF 12 CAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 2001:61843 CAPLUS
DOCUMENT NUMBER: 134:260866
TITLE: Identification of a novel class of small-molecule antiangiogenic agents through the screening of combinatorial libraries which function by inhibiting the binding and localization of proteinase MMP2 to integrin .alpha.V.beta.3
AUTHOR(S): Boger, Dale L.; Goldberg, Joel; Silletti, Steve; Kessler, Torsten; Cheresh, David A.
CORPORATE SOURCE: Departments of Chemistry Immunology and Vascular Biology, The Skaggs Institute for Chemical Biology The Scripps Research Institute, La Jolla, CA, 92037, USA
SOURCE: Journal of the American Chemical Society (2001), 123(7), 1280-1288
CODEN: JACSAT; ISSN: 0002-7863
PUBLISHER: American Chemical Society
DOCUMENT TYPE: Journal
LANGUAGE: English
OTHER SOURCE(S): CASREACT 134:260866

AB The process of new blood vessel growth from existing vasculature, known as angiogenesis, is crit. to several pathol. conditions, most notably cancer. Both MMP2, which degrades the extracellular matrix (ECM), and integrin .alpha.V.beta.3, which contributes to endothelial cell attachment to the ECM, are critically involved in this process. Recent findings have shown that MMP2 is localized in an active form on the surface of invasive endothelial cells based on its ability to directly bind integrin .alpha.V.beta.3, suggesting that disrupting this protein-protein interaction may represent a new target for the development of angiogenesis inhibitors. The screening of small mol. libraries led to the identification of compds. which disrupt the MMP2-.alpha.V.beta.3 interaction in an in vitro binding assay. A prototypical inhibitor was further found to prevent the degrdn. of the protein matrix without directly inhibiting MMP2 activity or disrupting the binding of .alpha.V.beta.3 to its classical ECM ligand, vitronectin. The synthesis and screening of analogs and substructures of this lead compd. allowed the identification of requisite structural features for inhibition of MMP2 binding to .alpha.V.beta.3. This led to the synthesis of a more water-sol. deriv. which maintains the in vitro biol. properties and has potent antiangiogenic and antitumor activity in vivo, validating the target as one useful for therapeutic intervention.

IT **331714-07-9P 331714-10-4P 331714-16-0P**
RL: BAC (Biological activity or effector, except adverse); BPR (Biological process); BSU (Biological study, unclassified); PRP (Properties); RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); PROC (Process); RACT (Reactant or reagent); USES (Uses)
(identification of novel class of small-mol. antiangiogenic agents through screening of combinatorial libraries)

RN 331714-07-9 CAPLUS
CN L-Lysine, 1,1'-(1,3-phenylenedicarbonyl)bis[N6-[N-[2-[[2-(4-fluorophenyl)ethyl]amino]-2-oxoethyl]glycyl]-N2-[[[4-(trifluoromethyl)phenyl]methoxy]carbonyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



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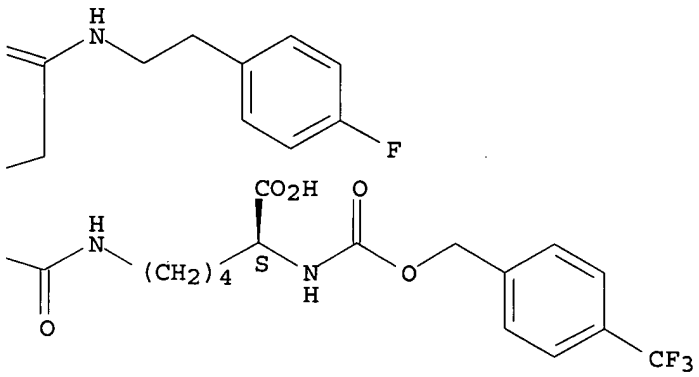


REFERENCE COUNT: 27 THERE ARE 27 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L9 ANSWER 8 OF 12 CAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 2001:47677 CAPLUS
DOCUMENT NUMBER: 134:246978
TITLE: Disruption of matrix **metalloproteinase** 2 binding to integrin .alpha.v.beta.3 by an organic molecule inhibits angiogenesis and tumor growth in vivo
AUTHOR(S): Silletti, Steve; Kessler, Torsten; Goldberg, Joel; Boger, Dale L.; Cheresh, David A.
CORPORATE SOURCE: Departments of Immunology and Vascular Biology, The Scripps Research Institute, La Jolla, CA, 92037, USA
SOURCE: Proceedings of the National Academy of Sciences of the United States of America (2001), 98(1), 119-124
CODEN: PNASA6; ISSN: 0027-8424
PUBLISHER: National Academy of Sciences
DOCUMENT TYPE: Journal
LANGUAGE: English

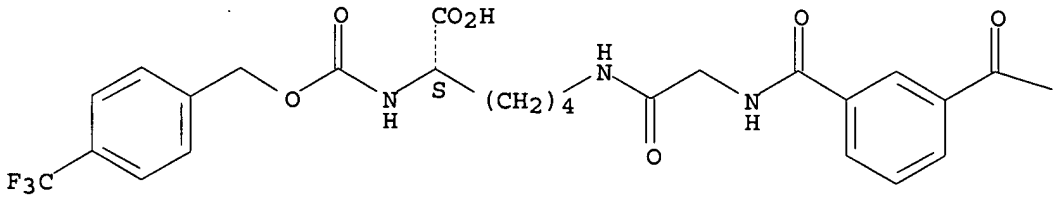
AB Matrix **metalloproteinase** 2 (MMP2) can assoc. with integrin .alpha.v.beta.3 on the surface of endothelial cells, thereby promoting vascular invasion. Here, we describe an org. mol. (TSRI265) selected for its ability to bind to integrin .alpha.v.beta.3 and block .alpha.v.beta.3 interaction with MMP2. Although disrupting .alpha.v.beta.3/MMP2 complex formation, TSRI265 has no effect on .alpha.v.beta.3 binding to its extracellular matrix ligand vitronectin and does not influence MMP2 activation or catalytic activity directly. However, TSRI265 acts as a potent antiangiogenic agent and thereby blocks tumor growth in vivo. These findings suggest that activated MMP2 does not facilitate vascular invasion during angiogenesis unless it forms a complex with .alpha.v.beta.3 on the endothelial cell surface. By disrupting endothelial cell invasion without broadly suppressing cell adhesion or MMP function, the use of compds. such as TSRI265 may provide a novel therapeutic approach for diseases assocd. with uncontrolled angiogenesis.

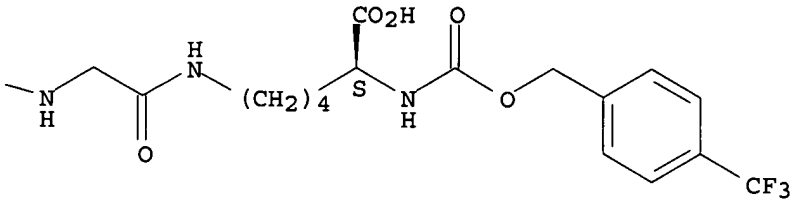
IT **331678-22-9**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(disruption of matrix **metalloproteinase** 2 binding to integrin .alpha.v.beta.3 by org. mol. (TSRI265), inhibits angiogenesis and tumor growth in vivo)

RN 331678-22-9 CAPLUS
CN L-Lysine, N6,N6'-[1,3-phenylenebis[carbonylimino(1-oxo-2,1-ethanediyl)]]bis[N2-[[[4-(trifluoromethyl)phenyl]methoxy]carbonyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A





REFERENCE COUNT: 22 THERE ARE 22 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L9 ANSWER 9 OF 12 CAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 2000:456916 CAPLUS
DOCUMENT NUMBER: 133:68929
TITLE: Use of a matrix **metalloproteinase** inhibitor and an integrin antagonist in the treatment of neoplasia
INVENTOR(S): McKearn, John P.; Gordon, Gary; Cunningham, James J.; Gately, Stephen T.; Koki, Alane T.; Masferrer, Jaime L.
PATENT ASSIGNEE(S): G. D. Searle & Co., USA
SOURCE: PCT Int. Appl., 358 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 12
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2000038719	A1	20000706	WO 1999-US30700	19991222
W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
CA 2356402	AA	20000706	CA 1999-2356402	19991222
EP 1140183	A1	20011010	EP 1999-968942	19991222
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JP 2002533407	T2	20021008	JP 2000-590670	19991222
ZA 2001005055	A	20020920	ZA 2001-5055	20010620
ZA 2001005120	A	20020107	ZA 2001-5120	20010621

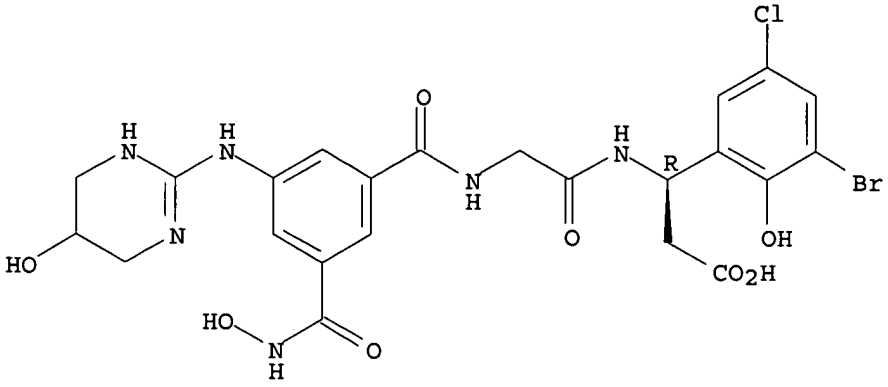
PRIORITY APPLN. INFO.: US 1998-113786P P 19981223
WO 1999-US30700 W 19991222

AB Methods are provided to treat or prevent neoplasia disorders in a mammal using a combination of a matrix **metalloproteinase** inhibitor, an integrin antagonist, and an antineoplastic agent.

IT **280105-14-8**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(matrix **metalloproteinase** inhibitor and integrin antagonist in neoplasia treatment)

RN 280105-14-8 CAPLUS
CN .beta.-Alanine, N-[3-[(hydroxyamino)carbonyl]-5-[(1,4,5,6-tetrahydro-5-hydroxy-2-pyrimidinyl)amino]benzoyl]glycyl-3-(3-bromo-5-chloro-2-hydroxyphenyl)-, (3R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



REFERENCE COUNT: 5 THERE ARE 5 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

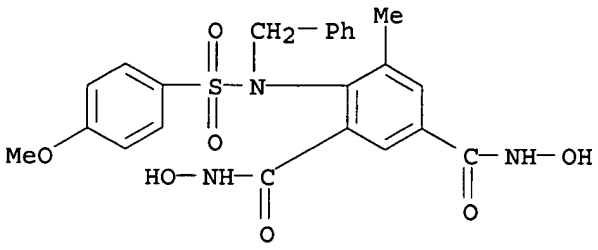
L9 ANSWER 10 OF 12 CAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 1999:495123 CAPLUS
DOCUMENT NUMBER: 131:129760
TITLE: Preparation of sulfonamidobenzenehydroxamates and analogs as matrix **metalloproteinase** and TACE inhibitors
INVENTOR(S): Levin, Jeremy Ian; Du, Mila T.; Venkatesan, Aranapakam Mudumbai; Nelson, Frances Christy; Zask, Arie; Gu, Yansong
PATENT ASSIGNEE(S): American Cyanamid Co., USA
SOURCE: U.S., 68 pp.
CODEN: USXXAM
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 5929097	A	19990727	US 1997-944593	19971006

PRIORITY APPLN. INFO.: US 1996-28504P P 19961016
OTHER SOURCE(S): MARPAT 131:129760

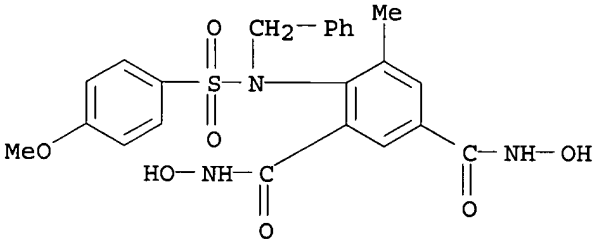
AB RSO2N(CH2R7)ZCONHOH [I; R = (un)substituted (hetero)aryl; R7 = H, alkyl, Ph, etc.; Z = (un)substituted phenylene or -naphthylene] were prepd. Thus, 2-(H2N)C6H4CO2Me was amidated by 4-(MeO)C6H4SO2Cl and the N-benzylated product converted in 2 steps to I [R = C6H4(OMe)-4, R7 = Ph, Z = 1,2-phenylene]. Data for biol. activity of I were given.

IT **206549-45-3P**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(prepn. of sulfonamidobenzenehydroxamates and analogs as matrix **metalloproteinase** and TACE inhibitors)
RN 206549-45-3 CAPLUS
CN 1,3-Benzenedicarboxamide, N,N'-dihydroxy-4-[[(4-methoxyphenyl)sulfonyl](phenylmethyl)amino]-5-methyl-, disodium salt (9CI) (CA INDEX NAME)



●2 Na

IT **206549-44-2P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(prepn. of sulfonamidobenzenehydroxamates and analogs as matrix **metalloproteinase** and TACE inhibitors)
RN 206549-44-2 CAPLUS
CN 1,3-Benzenedicarboxamide, N,N'-dihydroxy-4-[[(4-methoxyphenyl)sulfonyl](phenylmethyl)amino]-5-methyl- (9CI) (CA INDEX NAME)



REFERENCE COUNT: 19 THERE ARE 19 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L9 ANSWER 11 OF 12 CAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 1999:96248 CAPLUS
DOCUMENT NUMBER: 130:148689
TITLE: Phosphonated agents and their antiangiogenic and antitumorigenic use
INVENTOR(S): Collins, Delwood C.; Gagliardi, Antonio R.; Nickel, Peter
PATENT ASSIGNEE(S): University of Kentucky Research Foundation, USA
SOURCE: PCT Int. Appl., 74 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9905148	A1	19990204	WO 1998-US15470	19980724
W: AU, CA, JP, MX				
RW: AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
AU 9885915	A1	19990216	AU 1998-85915	19980724
AU 739637	B2	20011018		
EP 1019419	A1	20000719	EP 1998-937133	19980724
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI				

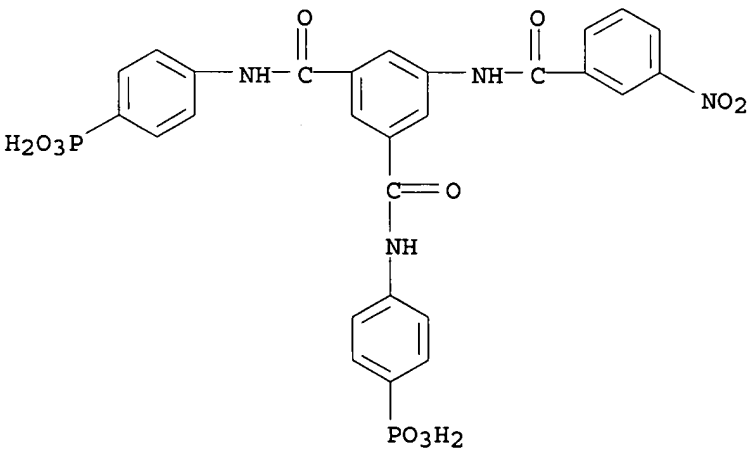
PRIORITY APPLN. INFO.: US 1997-899996 A 19970724
WO 1998-US15470 W 19980724
OTHER SOURCE(S): MARPAT 130:148689

AB The present invention relates to novel phosphonic acid substituted agents and their pharmaceutical compns. Phosphonic acid substituted agents that are potent inhibitors of angiogenesis or tumorigenesis is defined by the following formula: (P-Yn1)m1-Q1-K-(Q2-(Yn2-P)m2)j (P = phosphonic group, phosphonic salt; Y = OCO, NR1CO, CON(R1)R2; Q1, Q2 = aryl; K = H, NHCONH, NHCSNH, NHCOR3, NHCSR3CSNH; j, n1, n2 = 0-2; m1, m2 = 1-4; R1 = H, CH2CO2H, alkyl; R2 = alkyl, aryl, alkaryl; R3 = aryl). A pharmaceutical compn. for the treatment of angiogenesis-dependent conditions or tumors comprises an effective amt. of a phosphonic acid agent and a pharmaceutically acceptable carrier. Some of the phosphonic acid agents were more potent inhibitors of angiogenesis in the chick chorioallantoic membrane (CAM) assay and to human microvascular endothelial cell growth than suramin.

IT **220240-01-7**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(phosphonic acid agents and their antiangiogenic and antitumorigenic use)

RN 220240-01-7 CAPLUS

CN Phosphonic acid, [[5-[(3-nitrobenzoyl)amino]-1,3-phenylene]bis(carbonylimino-4,1-phenylene)]bis-, disodium salt (9CI) (CA INDEX NAME)



●2 Na

REFERENCE COUNT: 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L9 ANSWER 12 OF 12 CAPLUS COPYRIGHT 2003 ACS on STN

ACCESSION NUMBER: 1998:251153 CAPLUS

DOCUMENT NUMBER: 128:308308

TITLE: The preparation and use of ortho-sulfonamido aryl hydroxamic acids as matrix **metalloproteinase** and TACE inhibitors

INVENTOR(S): Levin, Jeremy Ian; Du Mila, T.; Venkatesan, Aranapakam Mudumbai; Nelson, Frances Christy; Zask, Arie; Gu, Yansong

PATENT ASSIGNEE(S): American Cyanamid Company, USA

SOURCE: PCT Int. Appl., 164 pp.
CODEN: PIXXD2

DOCUMENT TYPE: Patent

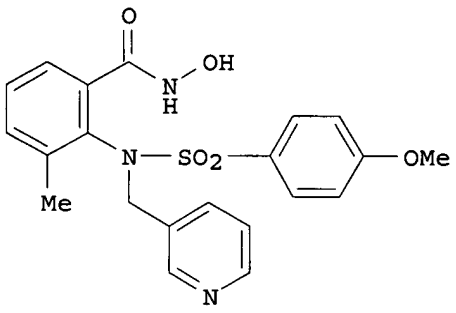
LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE

WO 9816503 A2 19980423 WO 1997-US18280 19971008
W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, HU, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, UZ, VN, YU, ZW
RW: GH, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG
AU 9851458 A1 19980511 AU 1998-51458 19971008
AU 731737 B2 20010405
EP 938471 A1 19990901 EP 1997-946246 19971008
EP 938471 B1 20011212
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, PT, IE, SI, LT, LV, FI, RO
BR 9712525 A 19991019 BR 1997-12525 19971008
CN 1240429 A 20000105 CN 1997-180613 19971008
JP 2001504809 T2 20010410 JP 1998-518448 19971008
AT 210637 E 20011215 AT 1997-946246 19971008
ES 2166102 T3 20020401 ES 1997-946246 19971008
ZA 9709233 A 19990415 ZA 1997-9233 19971015
TW 410220 B 20001101 TW 1997-86114187 19971015
KR 2000049196 A 20000725 KR 1999-703294 19990415
HK 1021178 A1 20020404 HK 2000-100090 20000106
PRIORITY APPLN. INFO.: US 1996-732631 A 19961016
WO 1997-US18280 W 19971008
OTHER SOURCE(S): MARPAT 128:308308
GI



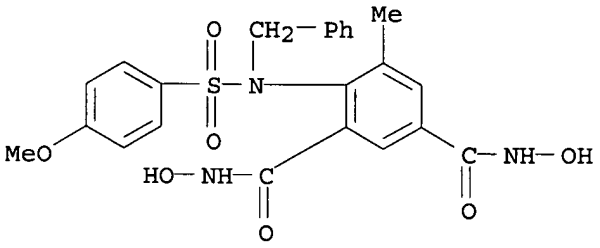
II

AB The invention relates to novel, low mol. wt., non-peptide inhibitors of matrix metalloproteinases (e.g. gelatinases, stromelysins and collagenases) and TNF-.alpha. converting enzyme (TACE, tumor necrosis factor-.alpha. converting enzyme). The compds. are useful for the treatment of diseases in which these enzymes are implicated such as arthritis, tumor growth and metastasis, angiogenesis, tissue ulceration, abnormal wound healing, periodontal disease, bone disease, proteinuria, aneurysmal aortic disease, degenerative cartilage loss following traumatic joint injury, demyelinating diseases of the nervous system, graft rejection, cachexia, anorexia, inflammation, fever, insulin resistance, septic shock, congestive heart failure, inflammatory disease of the central nervous system, inflammatory bowel disease, HIV infection, age related macular degeneration, diabetic retinopathy, proliferative vitreoretinopathy, retinopathy of prematurity, ocular inflammation, keratoconus, Sjogren's syndrome, myopia, ocular tumors, and ocular angiogenesis/neovascularization. The invention compds. are represented by the formula ZSO2N(CH2R7)ACONHOH [I; A = (un)substituted Ph or naphthyl; Z = (un)substituted aryl, heteroaryl, or benzo-fused heteroaryl; R7 = H, (un)substituted alk(en/yn)yl, Ph, naphthyl, 5- or 6-membered heteroaryl, cycloalkyl, or cycloheteroalkyl; or R7CH2NA forms a non-arom. 1,2-benzo-fused 7- to 10-membered heterocyclic ring with an optional addn. benzo fusion; where the hydroxamic acid moiety and the sulfonamido moiety are bonded to adjacent carbons on group A], and include pharmaceutically

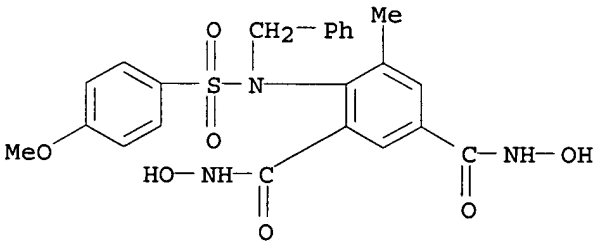
acceptable salts, optical [redacted]mers, and diastereomers. Prep[redacted] of over 400 compds., including I and th[redacted]r intermediates, are given. For instance, 2-[(4-methoxybenzenesulfonyl)amino]-3-methylbenzoic acid Me ester (prepn. given) was N-alkylated by 3-picolyl chloride-HCl (83%), followed by hydrolysis of the ester with LiOH in aq. THF (100%), activation with oxalyl chloride, and hydroxamidation with NH2OH.HCl (51%), to give title compd. II. At 50 mg/kg/day in rats with cartilage implants, II gave 44.6% inhibition of cartilage wt. loss, and 51.2% inhibition of cartilage collagen loss.

IT **206549-44-2P 206549-45-3P**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(prepn. of ortho-sulfonamido aryl hydroxamic acids as matrix **metalloproteinase** and TACE inhibitors)

RN 206549-44-2 CAPLUS
CN 1,3-Benzenedicarboxamide, N,N'-dihydroxy-4-[[(4-methoxyphenyl)sulfonyl](phenylmethyl)amino]-5-methyl- (9CI) (CA INDEX NAME)



RN 206549-45-3 CAPLUS
CN 1,3-Benzenedicarboxamide, N,N'-dihydroxy-4-[[(4-methoxyphenyl)sulfonyl](phenylmethyl)amino]-5-methyl-, disodium salt (9CI) (CA INDEX NAME)



●2 Na

=> file stnguide

COST IN U.S. DOLLARS	SINCE FILE ENTRY	TOTAL SESSION
FULL ESTIMATED COST	57.82	229.27
DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS)	SINCE FILE ENTRY	TOTAL SESSION
CA SUBSCRIBER PRICE	-7.81	-9.11

FILE 'STNGUIDE' ENTERED AT 10:35:40 ON 16 OCT 2003

L19 ANSWER 3 OF 5 CAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 2000:335229 CAPLUS
DOCUMENT NUMBER: 132:343358
TITLE: Cystine derivatives as therapeutic agents for matrix metalloprotease-related diseases
INVENTOR(S): Grams, Frank; Krell, Hans-Willi; Leinert, Herbert; Zimmermann, Gerd
PATENT ASSIGNEE(S): Roche Diagnostics G.m.b.H., Germany
SOURCE: PCT Int. Appl., 20 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2000027378	A2	20000518	WO 1999-EP8460	19991105
WO 2000027378	A3	20010920		
W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
BR 9915127	A	20010731	BR 1999-15127	19991105
EP 1143960	A2	20011017	EP 1999-971709	19991105
EP 1143960	A3	20011205		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
JP 2002529404	T2	20020910	JP 2000-580607	19991105
ZA 2001003605	A	20011211	ZA 2001-3605	20010504

PRIORITY APPLN. INFO.: EP 1998-121073 A 19981106
WO 1999-EP8460 W 19991105

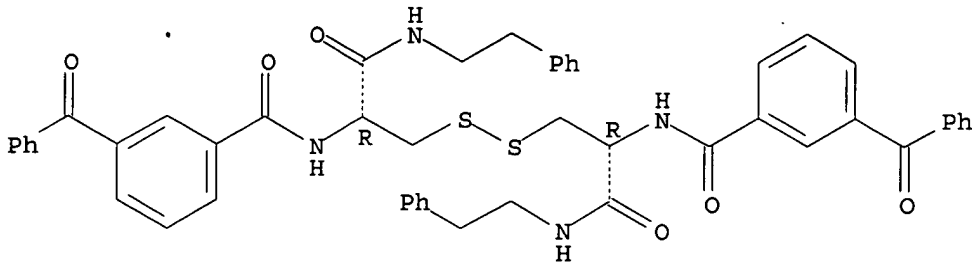
OTHER SOURCE(S): MARPAT 132:343358

AB Pharmaceutical compns. are disclosed which contain nonpeptidic cystine derivs. R1ANHCH[CH2SSCH2CH(R3ANH)(C(O)NHR4)]C(O)NHR2 [R1, R3 = H, (non)arom. carbocyclic or **heterocyclic** ring, (un)branched (un)satd. C1-15 alkyl which can be interrupted by **hetero** atom and which can be substituted by (non)arom. carbocyclic or **heterocyclic** ring; R2, R4 = H, (un)branched (un)satd. C1-15 alkyl which can be interrupted by **hetero** atom and which can be substituted by (non)arom. carbocyclic or **heterocyclic** ring; A = valency bond, CO, SO2, NHCO, NHCS or OC(O)], their pharmacol. acceptable salts and optically active forms thereof and pharmaceutically acceptable carriers, for the treatment of diseases selected from tumor growth and metastasis; inflammatory diseases, e.g. osteo- and rheumatoid arthritis; osteoporosis; multiple sclerosis; periodontitis; restenosis; diseases caused by bacteria, e.g. meningitis; sun-induced skin aging; and Alzheimer's disease. New compds. are also disclosed.

IT **269067-09-6P 269067-10-9P 269067-11-0P**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(cystine deriv. for treatment of matrix metalloprotease-related disease)

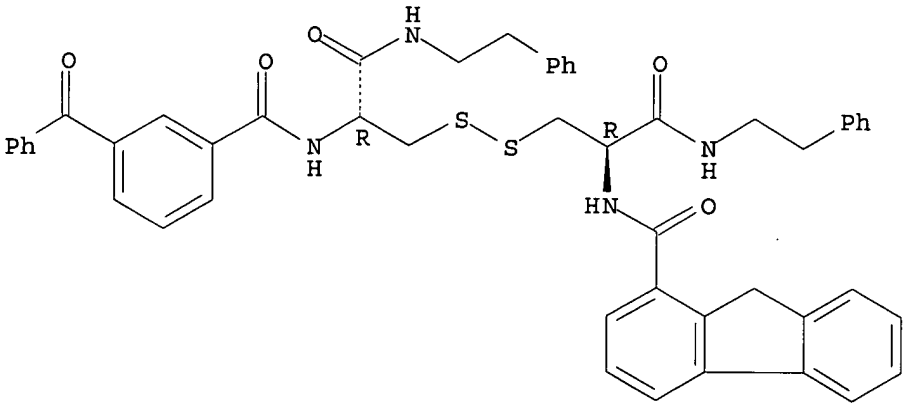
RN 269067-09-6 CAPLUS
CN Benzamide, N,N'-[dithiobis[(1R)-1-[[(2-phenylethyl)amino]carbonyl]-2,1-ethanediyl]]bis[3-benzoyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



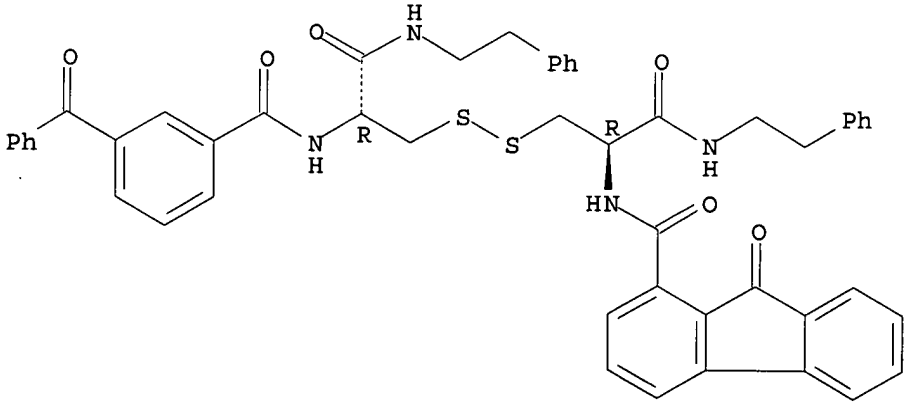
RN 269067-10-9 CAPLUS
CN 9H-Fluorene-1-carboxamide, N-[(1R)-1-[[[(2R)-2-[(3-benzoylbenzoyl)amino]-3-oxo-3-[(2-phenylethyl)amino]propyl]dithio]methyl]-2-oxo-2-[(2-phenylethyl)amino]ethyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 269067-11-0 CAPLUS
CN 9H-Fluorene-1-carboxamide, N-[(1R)-1-[[[(2R)-2-[(3-benzoylbenzoyl)amino]-3-oxo-3-[(2-phenylethyl)amino]propyl]dithio]methyl]-2-oxo-2-[(2-phenylethyl)amino]ethyl]-9-oxo- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L19 ANSWER 4 OF 5 CAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 1999:495123 CAPLUS
DOCUMENT NUMBER: 131:129760
TITLE: Preparation of sulfonamidobenzenehydroxamates and analogs as matrix **metalloproteinase** and TACE inhibitors
INVENTOR(S): Levin, Jeremy Ian; Du, Mila T.; Venkatesan, Aranapakam Mudumbai; Nelson, Frances Christy; Zask, Arie; Gu, Yansong
PATENT ASSIGNEE(S): American Cyanamid Co., USA

SOURCE: U.S., [redacted]pp.
CODEN: USXXAM
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

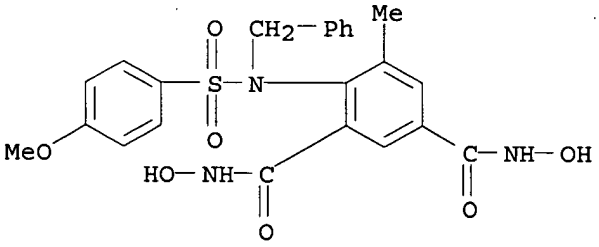
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 5929097	A	19990727	US 1997-944593	19971006

PRIORITY APPLN. INFO.: US 1996-28504P P 19961016
OTHER SOURCE(S): MARPAT 131:129760

AB RSO2N(CH2R7)ZCONHOH [I; R = (un)substituted (**hetero**)aryl; R7 = H, alkyl, Ph, etc.; Z = (un)substituted phenylene or -naphthylene] were prepd. Thus, 2-(H2N)C6H4CO2Me was amidated by 4-(MeO)C6H4SO2Cl and the N-benzylated product converted in 2 steps to I [R = C6H4(OMe)-4, R7 = Ph, Z = 1,2-phenylene]. Data for biol. activity of I were given.

IT **206549-45-3P**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(prepn. of sulfonamidobenzenehydroxamates and analogs as matrix **metalloproteinase** and TACE inhibitors)

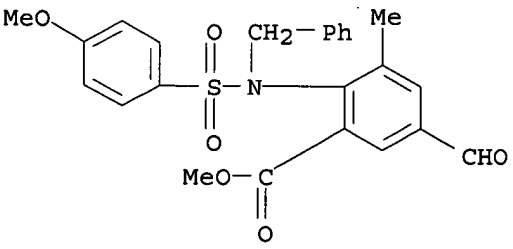
RN 206549-45-3 CAPLUS
CN 1,3-Benzenedicarboxamide, N,N'-dihydroxy-4-[[(4-methoxyphenyl)sulfonyl](phenylmethyl)amino]-5-methyl-, disodium salt (9CI) (CA INDEX NAME)



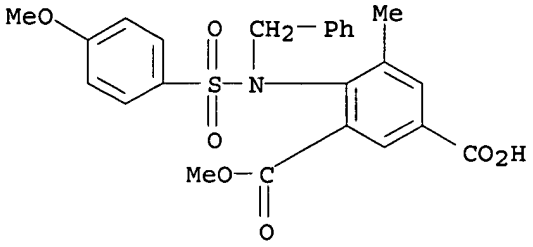
●2 Na

IT **206549-41-9P 206549-42-0P 206549-43-1P**
206549-44-2P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(prepn. of sulfonamidobenzenehydroxamates and analogs as matrix **metalloproteinase** and TACE inhibitors)

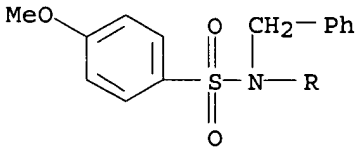
RN 206549-41-9 CAPLUS
CN Benzoic acid, 5-formyl-2-[[(4-methoxyphenyl)sulfonyl](phenylmethyl)amino]-3-methyl-, methyl ester (9CI) (CA INDEX NAME)

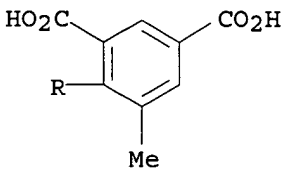


RN 206549-42-0 CAPLUS
CN 1,3-Benzenedicarboxylic acid, 4-[[(4-methoxyphenyl)sulfonyl](phenylmethyl)amino]-5-methyl-, 3-methyl ester (9CI) (CA INDEX NAME)

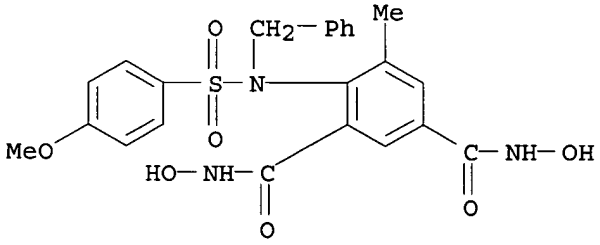


RN 206549-43-1 CAPLUS
CN 1,3-Benzenedicarboxylic acid, 4-[[(4-methoxyphenyl)sulfonyl](phenylmethyl)amino]-5-methyl- (9CI) (CA INDEX NAME)





RN 206549-44-2 CAPLUS
CN 1,3-Benzenedicarboxamide, N,N'-dihydroxy-4-[[(4-methoxyphenyl)sulfonyl](phenylmethyl)amino]-5-methyl- (9CI) (CA INDEX NAME)



REFERENCE COUNT: 19 THERE ARE 19 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L19 ANSWER 5 OF 5 CAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 1998:251153 CAPLUS
DOCUMENT NUMBER: 128:308308
TITLE: The preparation and use of ortho-sulfonamido aryl hydroxamic acids as matrix **metalloproteinase** and TACE inhibitors
INVENTOR(S): Levin, Jeremy Ian; Du Mila, T.; Venkatesan, Aranapakam Mudumbai; Nelson, Frances Christy; Zask, Arie; Gu, Yansong
PATENT ASSIGNEE(S): American Cyanamid Company, USA
SOURCE: PCT Int. Appl., 164 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1

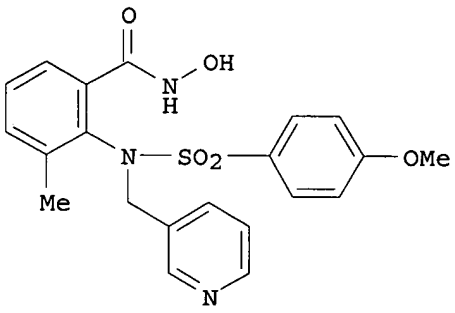
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9816503	A2	19980423	WO 1997-US18280	19971008
W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, HU, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, UZ, VN, YU, ZW				
RW: GH, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
AU 9851458	A1	19980511	AU 1998-51458	19971008
AU 731737	B2	20010405		
EP 938471	A1	19990901	EP 1997-946246	19971008
EP 938471	B1	20011212		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, PT, IE, SI, LT, LV, FI, RO				
BR 9712525	A	19991019	BR 1997-12525	19971008
CN 1240429	A	20000105	CN 1997-180613	19971008
JP 2001504809	T2	20010410	JP 1998-518448	19971008
AT 210637	E	20011215	AT 1997-946246	19971008
ES 2166102	T3	20020401	ES 1997-946246	19971008
ZA 9709233	A	19990415	ZA 1997-9233	19971015
TW 410220	B	20001101	TW 1997-86114187	19971015
KR 2000049196	A	20000725	KR 1999-703294	19990415
HK 1021178	A1	20020404	HK 2000-100090	20000106

PRIORITY APPLN. INFO.: US 1996-732631 A 19961016
WO 1997-US18280 W 19971008

OTHER SOURCE(S): MARPAT 128:308308

GI



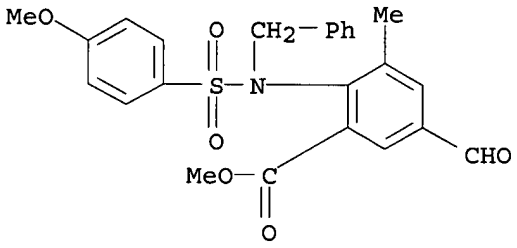
II

AB The invention relates to novel, low mol. wt., non-peptide inhibitors of matrix metalloproteinases (e.g. gelatinases, stromelysins and collagenases) and TNF-.alpha. converting enzyme (TACE, tumor necrosis factor-.alpha. converting enzyme). The compds. are useful for the treatment of diseases in which these enzymes are implicated such as arthritis, tumor growth and metastasis, angiogenesis, tissue ulceration, abnormal wound healing, periodontal disease, bone disease, proteinuria, aneurysmal aortic disease, degenerative cartilage loss following traumatic joint injury, demyelinating diseases of the nervous system, graft rejection, cachexia, anorexia, inflammation, fever, insulin resistance, septic shock, congestive heart failure, inflammatory disease of the central nervous system, inflammatory bowel disease, HIV infection, age related macular degeneration, diabetic retinopathy, proliferative vitreoretinopathy, retinopathy of prematurity, ocular inflammation, keratoconus, Sjogren's syndrome, myopia, ocular tumors, and ocular angiogenesis/neovascularization. The invention compds. are represented by the formula ZSO2N(CH2R7)ACONHOH [I; A = (un)substituted Ph or naphthyl; Z = (un)substituted aryl, **heteroaryl**, or benzo-fused **heteroaryl**; R7 = H, (un)substituted alk(en/yn)yl, Ph, naphthyl, 5- or 6-membered **heteroaryl**, cycloalkyl, or cycloheteroalkyl; or R7CH2NA forms a non-arom. 1,2-benzo-fused 7- to 10-membered

heterocyclic ring with an additional addn. benzo fusion; where the hydroxamic acid moiety and the sulfonamido moiety are bonded to adjacent carbons on group A], and include pharmaceutically acceptable salts, optical isomers, and diastereomers. Prepns. of over 400 compds., including I and their intermediates, are given. For instance, 2-[(4-methoxybenzenesulfonyl)amino]-3-methylbenzoic acid Me ester (prepn. given) was N-alkylated by 3-picolyl chloride-HCl (83%), followed by hydrolysis of the ester with LiOH in aq. THF (100%), activation with oxalyl chloride, and hydroxamidation with NH2OH.HCl (51%), to give title compd. II. At 50 mg/kg/day in rats with cartilage implants, II gave 44.6% inhibition of cartilage wt. loss, and 51.2% inhibition of cartilage collagen loss.

IT **206549-41-9P 206549-42-0P 206549-43-1P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(intermediate; prepn. of ortho-sulfonamido aryl hydroxamic acids as matrix **metalloproteinase** and TACE inhibitors)

RN 206549-41-9 CAPLUS
CN Benzoic acid, 5-formyl-2-[[(4-methoxyphenyl)sulfonyl](phenylmethyl)amino]-3-methyl-, methyl ester (9CI) (CA INDEX NAME)



RN 206549-42-0 CAPLUS
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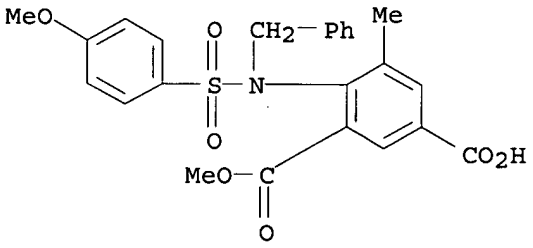

RN 206549-43-1 CAPLUS
CN 1,3-Benzenedicarboxylic acid, 4-[[(4-methoxyphenyl)sulfonyl](phenylmethyl)amino]-5-methyl- (9CI) (CA INDEX NAME)